ETIOLOGY AND CLINICAL OUTCOME OF STROKE IN YOUNG ADULTS (18-45YEARS) ADMITTED IN A TERTIARY CARE HOSPITAL

Dissertation submitted to

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI

In fulfilment of the regulations for the award of the degree of

Doctor of Medicine in General Medicine

DEPARTMENT OF GENERAL MEDICINE

P.S.G INSTITUTE OF MEDICAL SCIENCES & RESEARCH

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY,

CHENNAI, TAMIL NADU

APRIL 2016

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Dissertation submitted to

The Tamil Nadu Dr. M.G.R Medical University, Chennai

In fulfilment of the requirements for the award of the degree of

Doctor of Medicine in General Medicine

Under the guidance of

PROFESSOR S.SUJITH KUMAR M.D

DEPARTMENT OF GENERAL MEDICINE

P.S.G INSTITUTE OF MEDICAL SCIENCES & RESEARCH, COIMBATORE

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY,

CHENNAI, TAMIL NADU

APRIL 2016

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled, "**ETIOLOGY AND CLINICAL OUTCOME OF STROKE IN YOUNG ADULTS (18-45 YEARS) ADMITTED IN A TERTIARY CARE HOSPITAL"** is the bonafide original work of **Dr. KARRI MADHAVI** in fulfilment of the requirements for the degree of Doctor of Medicine in General Medicine

Signature of the guide

Dr. S.SUJITH KUMAR, MD
Professor of Medicine
Department of General Medicine
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ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled, "**ETIOLOGY AND CLINICAL OUTCOME OF STROKE IN YOUNG ADULTS (18-45 YEARS) ADMITTED IN A TERTIARY CARE HOSPITAL"** is the bonafide original research work of **Dr. KARRI MADHAVI** under the guidance of **Dr S.SUJITH KUMAR, M.D**, Professor of Medicine, P.S.G IMS&R, Coimbatore in partial fulfilment of the requirements for the degree of Doctor of Medicine in General Medicine.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**ETIOLOGY AND CLINICAL OUTCOME OF STROKE IN YOUNG ADULTS (18-45 YEARS) ADMITTED IN A TERTIARY CARE HOSPITAL"** is a bonafide and genuine research work carried out by me under the guidance of **Dr.S. SUJITH KUMAR, M.D,** Professor of Medicine, P.S.G IMS&R, Coimbatore.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University in fulfilment of the University regulations for the award of MD degree in General Medicine. This dissertation has not been submitted for award of any other degree or diploma.

Signature of the Candidate

Dr. KARRI MADHAVI

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July 10, 2014

To
Dr Karri Madhavi
Postgraduate
Department of General Medicine
PSG IMS&R
Coimbatore

Ref.: Proposal titled: *"Etiology and clinical outcome of stroke in young adults (18 - 45 years) admitted in a tertiary care hospital"*

Sub.: Ethics Committee Approval for the study

The Institutional Human Ethics Committee, PSG IMS & R, Coimbatore -4, has reviewed your proposal on 24th June, 2014 in its full board review meeting held at Research Conference Hall, PSG IMS&R, between 2.00 pm and 4.45 pm, and discussed your application to conduct the study entitled:

"Etiology and clinical outcome of stroke in young adults (18 - 45 years) admitted in a tertiary care hospital"

The following documents were received for review:

1. Duly filled application form
2. Proposal
3. Informed Consent forms
4. Data Collection Tool
5. Permission letter from concerned Head of Department
6. CV
7. Budget

The members who attended the meeting at which your study proposal was discussed are as follows:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
2	Mrs. Geetha S Kannan	+ 2	Lay person	Female	No	Yes
3	Mr Gowpathy Velappan	BA., BL	Legal Advisor	Male	No	Yes
4	Mrs G Malarvizhi	M Sc	Nursing	Female	Yes	Yes
5	Mr. R. Nandakumar (Vice-Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
6	Dr. G. Rajendiran	DM	Clinician (Cardiology)	Male	Yes	No
7	Dr. V. Ramamurthy	Ph D	Biotechnology	Male	Yes	No

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8	Dr. M. Ramanathan	M Pharm, Ph D	Non-Medical (Pharmacy)	Male	Yes	Yes
9	Dr. P. Sathyan (Chairperson, IHEC)	DO, DNB	Clinician (Opthalmology)	Male	No	Yes
10	Dr. Seetha Panicker	MD	Clinician (Obstetrics & Gyanaecology)	Female	Yes	Yes
11	Dr. S. Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
12	Dr. Y.S. Sivan	Ph D	Social Scientist (Sociology)	Male	Yes	Yes
13	Dr. Sudha Ramalingam (Alternate Member-Secretary, IHEC)	MD	Public Health, Epidemiology, Genetics, Ethicist	Female	Yes	Yes
14	Mrs. K. Uma Maheswari	M Sc, M Phil. B Ed	Botany	Female	No	No
15	Dr. D. Vijaya	M Sc, Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

After due consideration, the committee has decided to approve the above proposal.

The approval is valid for one year.

We request you to intimate the date of initiation of the study to IHEC, PSG IMS&R and also, after completion of the project, please submit completion report to IHEC.

We hereby confirm that neither you nor any of your study team members have participated in the voting/ decision making procedure of the committee. The members of the committee who have participated in the voting/ decision making procedure of the committee do not have any conflict of interest in the referenced study.

This Ethics Committee is organized and operates according to Good Clinical Practice and Schedule Y requirements.

Non-adherence to the Standard Operating Procedures (SOP) of the Institutional Human Ethics Committee (IHEC) and national and international ethical guidelines shall result in withdrawal of approval (suspension or termination of the study). SOP will be revised from time to time and revisions are applicable prospectively to ongoing studies approved prior to such revisions.

PIs are required to send progress reports (in the form of an extended abstract with publications if any) to the IHEC every six months (and a month before expiry of approval date, if renewal of approval is being sought).

Request for renewal must be made at least a month ahead of the expiry of validity along with a copy of the progress report.

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Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Yours truly,

Dr Sudha Ramalingam
Alternate Member - Secretary
Institutional Human Ethics Committee

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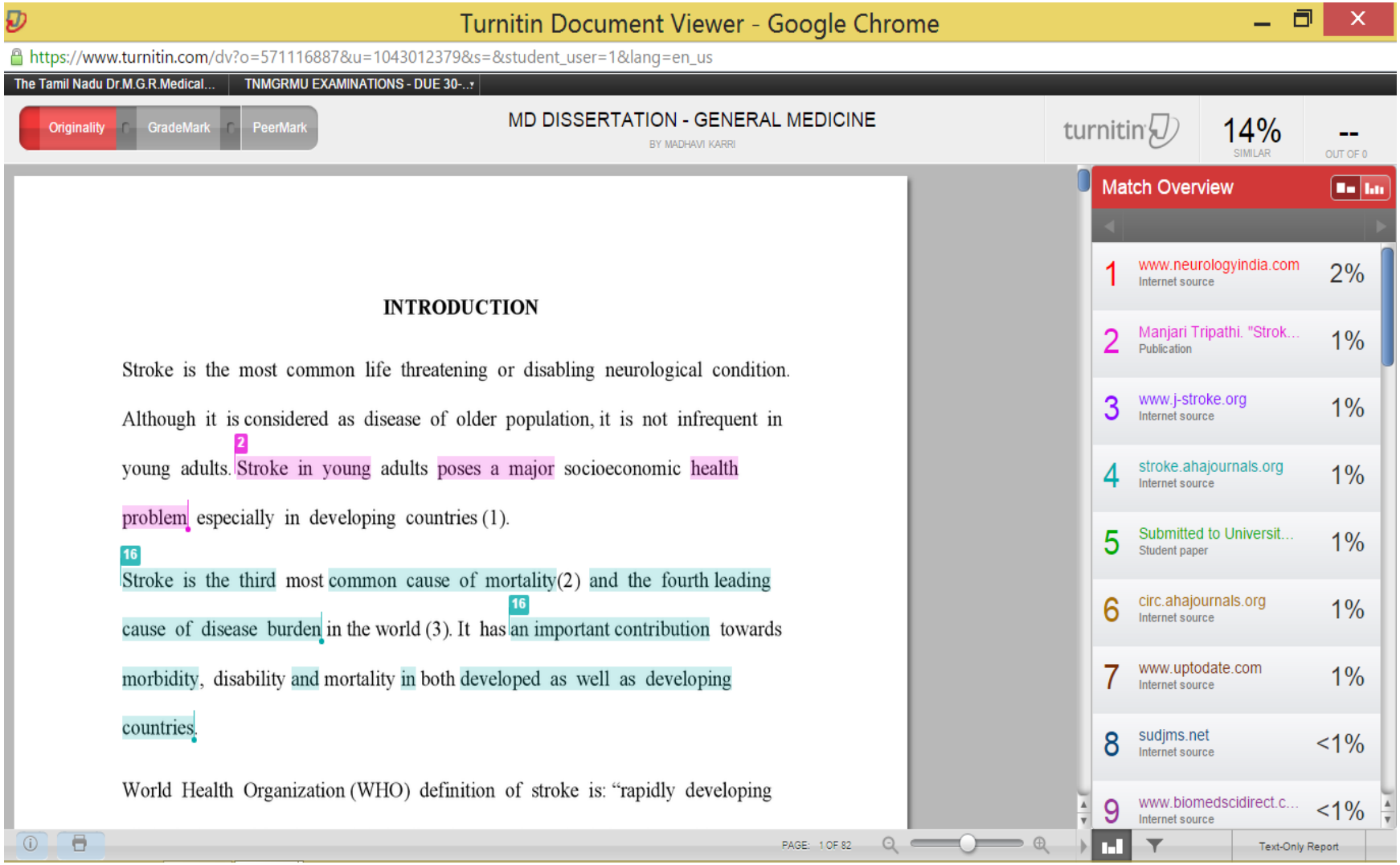
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INTRODUCTION
Stroke is the most common life threatening or disabling neurological condition. Although it is considered as disease of older population, it is not infrequent in young adults. Stroke in young adults poses a major socioeconomic health problem especially in developing countries (1).
Stroke is the third most common cause of mortality(2) and the fourth leading cause of disease burden in the world (3). It has an important contribution towards morbidity, disability and mortality in both developed as well as developing countries.
World Health Organization (WHO) definition of stroke is: "rapidly developing
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TITLE: **ETIOLOGY AND CLINICAL OUTCOME OF STROKE IN YOUNG ADULTS (18-45YEARS) ADMITTED IN A TERTIARY CARE HOSPITAL**

ABSTRACT :

Background : Stroke among young adults (18-45years) poses a major socioeconomic health problem especially in developing countries. It is an important cause of morbidity and mortality among young adults. This study was aimed to evaluate the etiology, risk factors and clinical outcome of arterial ischaemic stroke in young adults aged 18-45 years.

Materials and Methods: The study is based on prospective collection of data of young adults admitted in medical ward or neurology ward in a tertiary care hospital during the study period of June, 2014 to June, 2015. A proforma for each of the acute ischemic stroke patients was maintained. Data was analyzed using SPSS version 12. Chi-square was used. p value of <0.05 was considered to be significant.

Results: In this study, there were 36 males and 14 females with a mean (SD) age of 39.4 (9.5) years at onset of stroke. Smoking, alcohol intake and dyslipidemia were significantly more prevalent in the study group. An aetiological categorization of stroke was obtained in 39 (78%) patients and it was of unknown in the rest. Athero-thrombotic stroke and cardio-embolic stroke occurred in 40% and 16%, respectively. Hyperhomocystinemia also has a significant association with occurrence of stroke. Outcome assessment by using scoring scales (NIHSS and mRS at baseline and 3months),

after a follow up of 3 months, 50% of the study group (25) were independent or only mildly disabled. The fatality rate observed was 2%.

Conclusion: Ischaemic stroke in the young adult is more frequent in males. Modifiable risk factors – Smoking, alcohol and dyslipidemia were very common. Etiology can be determined in the majority and the athero-thrombotic process predominates. The mortality was negligible and the functional outcome is good in most of the patients.Thus, the knowledge of the risk factors and clinical presentation acute ischemic stroke in young adults can help in prevention, better understanding and therapeutic decision making in the disease management.

Keywords: Young adults, Arterial Ischemic Stroke, Risk factors

INTRODUCTION

Stroke is the most common life threatening or disabling neurological condition. Although it is considered as disease of older population, it is not infrequent in young adults. Stroke in young adults poses a major socioeconomic health problem especially in developing countries (1).

Stroke is the third most common cause of mortality(2) and the fourth leading cause of disease burden in the world(3).It has an important contribution towards morbidity, disability and mortality in both developed as well as developing countries.

World Health Organization (WHO) definition of stroke is: "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin."

Stroke leads to cut off of the oxygen and nutrients supply to the cerebral tissue leading to cerebral damage (1). The effects of a stroke depend on which part of the brain is injured and how severely it is affected. The most common symptom of a stroke is sudden weakness or numbness of the face, arm, or leg, most often on one side of the body, occurring in 90% of the strokes(4). Other symptoms include confusion; difficulty speaking or understanding speech; difficulty seeing with one or both eyes; difficulty walking, dizziness, and loss of balance

or coordination; severe headache with no known cause; fainting or unconsciousness.

It leaves the patients with residual disabilities like physical dependence, cognitive decline, depression, and seizures. A very severe stroke can cause sudden death.

The prevalence of various risk factors in stroke in young has been analysed in two studies from India(5). In a case control study of young stroke patients of age group 15-45 years with age- and sex-matched hospital and community controls, prevalence of various risk factors was studied. In another study in 1997(6),177 patients with first ever ischemic stroke (age group 15-45 years) were taken retrospectively based on hospital data, with 76% male and 24% female patients. Hypertension was present in 18% of the patients, whereas diabetes mellitus was present in 7% only. 69%of male patients were smokers. Dyslipidaemia in the form of elevated cholesterol was present in 17% and increase in triglycerides was observed in 42% patients.

A Study of Stroke among young adults in a Tertiary Hospital in North India - A retrospective review of case records from patients with ischemic stroke in the age range of 18-45 years was conducted from 2005 to 2010. Data regarding patients' clinical profiles, medical histories, diagnostic test results, and modified Rankin Scale scores at hospital discharge were examined. Stroke subtyping was conducted in accordance with the Trial of Org 10172 in

Acute Stroke Treatment (TOAST) criteria. 440 patients in the 18-45 year age range were identified with stroke out of which 83.4% were male. The most common risk factors were hypertension (34.4%) and dyslipidemia (26.5%). The most common subtype of stroke was undetermined (57%), followed by other determined causes (17.3%). Most of the patients demonstrated good functional outcomes. The results highlight the needs for aggressive management of traditional risk factors and extensive patient work-up to identify stroke etiology in India(7).

In a study on ischaemic stroke in young adults - Clinical features, risk factors and outcome was considered in the study done at Sri ChitraTirunal Institute of Medical Sciences and Technology, Trivandrum.This is a retrospective study done with medical records of 177 patients in a tertiary referral centre admitted between January 1988 and March 1994. Patients with ischaemic stroke were classified based on Trial on ORG 10172 in Acute Stroke Treatment (TOAST) criteria; out of which 25.2% patients had cardio-embolic stroke, 12.6% had large artery atherosclerosis and 7.5% had lacunar infarcts. Strokes due to other determined etiology were 11.2%. It was aimed to evaluate clinical features, risk factors and outcome of ischaemic stroke in young adults aged 15-45 years. It is more frequent in young males. Hypertension, smoking, hyperlipidaemia and athero-thrombotic stroke were significantly more prevalent. These cases were followed up at mean time of 7 months, 75% of

the patients were independent or only mildly disabled. The mortality observed was very little and functional outcome was good in most of the patients(8)

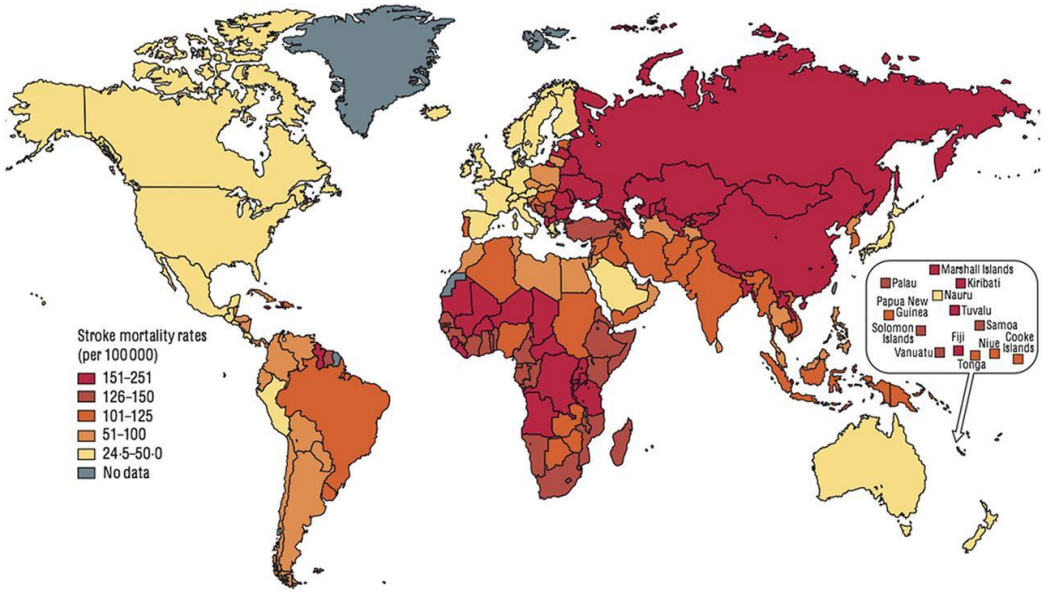
In Helsinki Young Stroke Registry(9) which included 1008 first ever consecutive patients of ischemic stroke in the age group of 15-49 years, admitted in 1994 to 2007. The etiology was classified by Trial of Org 10172 in Acute Stroke Treatment criteria. Comparisons were done between groups stratified by gender and age.Hypertension, smoking and dyslipidaemia with high total cholesterol emerged as important risk factors. The prevalence of hypertension increased with increasing age. It was also observed that, among the study population, preponderance of stroke was more among females with age of those <30, whereas males showed dominance with rapidly increased age of 44. The most frequent risk factors were dyslipidemia (60%), smoking (44%), and hypertension (39%). Left hemisphere infarcts were more common in general. The study was concluded saying that the frequency of ischemic stroke increases sharply at age 40. Subclinical infarcts were surprisingly common in the young.

It appears that the risk factors for stroke in Indian population are not different from that of the western or Southeast Asian population. The traditional risk factors like hypertension, smoking and diabetes are associated with stroke in both young and elderly. In recent years, there has been increasing economic and demographic development in

developing countries resulting in a shift from diseases caused by poverty towards chronic, non-communicable, lifestyle-related diseases(10). This happening in the younger age group adds to the social and economic burden, and as such these patients merit special attention in diagnostic, therapeutic, and preventive care.

A study was conducted to assess the clinical outcome in 287 consecutive young adults (15 to 45 years) with ischemic stroke by D. Leys MD et al.; and 3-year outcome was also observed in young patients admitted between 1992 and 1996 which was obtained with clinical examinations or telephone interviews, and data were recorded about risk factors, associated disorders, causes of stroke, and current treatments. In this study, young patients who experience ischemic strokes have a low risk of stroke recurrence and myocardial infarction(11).

FIGURE 1:



Therefore the need of this study is to reveal the burden of stroke in young adults in a tertiary care hospital, the frequency of aetiology of stroke in young adults with contributing risk factors and their effect on the clinical outcome of the patients of young stroke in tertiary care(12).

Early identification of risk factors and implication of preventive measures can help in bringing down the occurrence of stroke and reduce the financial and emotional burden in the family. A dedicated evaluation for identifying the cause is needed to treat and prevent further recurrences.

AIMS AND OBJECTIVES

- To study the aetiology and clinical outcome of stroke in young adults (18-45years) in a tertiary care centre.
- To assess the morbidity and mortality of the stroke in young adults.

MATERIALS AND METHODOLOGY

Type of study: Prospective and clinical study

Place of study: PSG Hospitals, PSG IMS&R, Coimbatore

Duration of Study: One year (June 2014 – June 2015)

Study Population: Patients aged (18-45 years) diagnosed as stroke in Department of General Medicine and Neurology, meeting the inclusion criteria in PSG IMS &R, Coimbatore, during the study period of 1 year June 2014 to June 2015. Patient sample size is restricted to a total number of 50cases.

INCLUSION CRITERIA:

- Age between 18-45years
- Patients admitted in general medical ward/neurology ward with abrupt onset of focal neurological deficit of vascular origin (ischaemic or haemorrhagic) and persisting for more than 24hrs.

EXCLUSION CRITERIA

- Pregnant women or postpartum women within 30days
- Age less than 18years
- Age more than 45years
- Head trauma
- Neuro infections causing weakness
- Venous strokes
- CNS Tumours with weakness
- Subdural haemorrhage and haemorrhagic strokes

METHODOLOGY:

The study is based on prospective collection of data of young adults aged between 18-45years diagnosed as stroke who got admitted in medical ward or neurology ward in a tertiary care centre where systematic computer coding for registry is used.

Patients admitted at PSG hospitals, Coimbatore diagnosed with stroke confirmed with imaging at admission and meeting the inclusion criteria as mentioned above, during the study period of June, 2014 to June, 2015 are taken into consideration for the study. A proforma is prepared which included detailed history, clinical examination and requisite investigations available in the hospital. After taking informed consent from the patient, history and risk factors attributable to the stroke are collected in detail. Investigations like complete hemogram, routine urine analysis, blood sugar, serum elecctrolytes, serum creatinine, blood urea, serum homocysteine, chest X-ray, electrocardiogram, CT or MRI brain were done in all patients. Investigations like ANA profile, APLA were done in the patients as required.

According to the imaging done at the baseline and risk factors associated with the patient, the stroke subtypes classified accordingly by using classification developed for Trial of Org 10172 in Acute Stroke Treatment (TOAST).

TABLE 1:

TOAST Classification Of Subtypes Of Acute Ischemic Stroke
Large-artery atherosclerosis (embolus/thrombosis)
Cardioembolism (high-risk/medium-risk)
Small-vessel occlusion(lacunae)
Stroke of other determined etiology
Stroke of undetermined etiology a. Two or more causes identified b. Negative evaluation c. Incomplete evaluation

Patients are examined clinically in detail and their severity is being assessed by National Institute of Health stroke scale (NIHSS) at baseline.

TABLE 2: National Institute of Health stroke scale (NIHSS)

STROKE	STROKE SEVERITY
0	No stroke symptoms
1-4	Minor Stroke
5-15	Moderate Stroke
16-20	Moderate to Severe Stroke
21-42	Severe Stroke

To assess the clinical outcome of the patients, mRS scoring is done at the baseline and after 3 months and are correlated accordingly. This scale runs from 0-6, running from perfect health without symptoms to death. (TABLE 3)

SCORE	SYMPTOMS
• 0	No symptoms
• 1	No significant disability. Able to carry out all usual activities, despite some symptoms
• 2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
• 3	Moderate disability. Requires some help, but able to walk unassisted
• 4	Moderately severe disability. Unable to attend to own

	bodily needs without assistance, and unable to walk unassisted
• 5	- Severe disability. Requires constant nursing care and attention, bedridden, incontinent
• 6	-Dead

The results were analysed to assess the etiology, risk factors and clinical outcome in the patients diagnosed with stroke.

Statistical tools:

The data collected from the patients is tabulated using Microsoft Excel. The data are reported as the mean +/- SD or the median, depending on their distribution. The differences in quantitative variables between groups were assessed by means of the unpaired t test. Comparison between groups was made by the non-parametric Mann- Whitney test. ANOVA was used to assess the variables. The chi square test was used to assess the difference in categoric variables between groups.

Descriptive analysis is done using chi square test and statistical analysis and interpretation of the data collected is done by using SPSS version 20. p value of <0.05 using two tailed test was taken as being of significance for all statistical tests. All data were analysed with a statistical software package (SSPS version 16.0 for windows)

REVIEW OF LITERATURE

History and Background:

Stroke was first recognized by HIPPOCRATES (460 to 370 BC), father of medicine some 2400 years ago. Initially is was termed as apoplexy in Greek (meaning “struck down by violence”).

Johann Jacob Wepfer (1620–1695), the next well renowned person in the field of stroke. He studied on the corpses of deceased due to apoplexy, to know the cause of apoplexy. He discovered that blood supply might be disrupted to the brain in the deceased either due to blocked arteries in few or they had been massive bleeding into the brain tissue(13).

Rudolf Virchow known as father of modern pathology was the first to describe the mechanism of thrombo embolism as a major factor causing stroke. In the mid nineteenth century , he describes the term thrombosis which can detached to form embolus causing cardio-embolic stroke(14).

In the year 1928, apoplexy was subcategorised based on the cause. After which the term cerebrovascular accident has been come into norms. Recently in 2011, use of this term cerebrovascular accident has been discouraged reasoning that the connotation of fortuitousness carried by the word *accident* insufficiently highlights the modifiability of the underlying risk factors(15), (16). Now it is used as cerebrovascular incident interchangeably.

DEFINITION AND CLASSIFICATION:

Although more common in older adults, stroke also occurs in neonates, infants, children and young adults, resulting in significant morbidity and mortality(17). Stroke is a clinical syndrome which is classified broadly as:

- Ischaemic strokes – These are caused by sudden occlusion of arteries supplying the brain, either due to thrombus at the site of occlusion or formed in another part of circulation causing restriction of blood supply to the part of brain causing cerebral infarction. It accounts for 50-85% of all strokes worldwide(18).
- Haemorrhagic strokes –defined as bleed which occurs within substance of the brain, intracerebral haemorrhage or contained within the subarachnoid haemorrhage(19).
- Transient ischemic attacks (TIAs) are defined as temporary neurological deficit with symptoms lasting less than 24hrs and which is thought to be due to inadequate cerebral or ocular blood supply as a result of arterial or embolism associated with arterial, cardiac or haematological disease. It serves as a warning signal for impending stroke. It leaves no clinical or imaging tracing(20).

EPIDEMIOLOGY:

Stroke is now considered as the second most common cause of death worldwide in 2011, accounting for 6.2 million deaths (~11% of the total)(21).There in increasing prevalence of stroke in developing countries from past two decades(22) whereas decreasing trend is observed in developed countries.

In India, the prevalence of stroke is in increasing trend. The incidence of stroke increases exponentially from 30 years of age, and etiology varies by age. About two-thirds of strokes occur in those over the age of 65(23), (24). It has been observed now that the prevalence is becoming high among younger age group and low socioeconomic status(25)

As there is increasing prevalence and incidence rates of stroke among older individuals, these is also increase in the prevalence of stroke in younger individuals (18-32% of all stroke cases) compared to that among the western countries.When considering the annual incidence rates of arterial ischemic stroke (AIS) in adults younger than 45 years old, incidence ranges from 3.4 to 11.3/100,000 people per year in primarily white populations (26)(27), while the incidence in young black adults is as high as 22.8/100,000 people per year(28).Indian Council Medical Research (ICMR) estimated in 2004 there were 9,30,985 cases of stroke in India with 6,39,455(41%) deaths and 6.4 million (72%) disability life adjusted years (DALY) lost(29).

This increase in prevalence and incidence is most likely due to rapid urbanisation among the villagers who migrated to urban areas, changing lifestyles, sedentary habits, smoking, excess alcohol intake, rising stress levels in life, etc(30).

Risk factors:

Risk factors are defined as any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury. Risk factors may be further classified as modifiable or non-modifiable.

Non modifiable risk factors:

Risk factors like age, gender, race/ethinicity and family genetics come under non modifiable risk factors.

1. **Gender:** Considering globally, males are affected predominantly regardless of age and stroke subtype. In Indian scenario, this difference observed is due to high prevalence of smoking and alcohol among males comparatively. The male : female sex ratio among affected individuals is 7:1 in India(31)(32)

   Few etiologies are confined only to the female population. Most of the strokes are observed commonly among the reproductive age group due to pregnancy or oral contraceptive usage. Though prevalence of occurrence of stroke is high among males, prevalence of death is high among females comparatively.

2. **Race and ethnicity:** blacks are more commonly affected with stroke compared to whites. Lack of proper awareness, affordability and no insurance are few among factors due to this observed difference in occurrence of stroke(33)(34).
3. **Family genetics:** Family members may have genetic tendency or share lifestyles and behavioural patterns that significantly contribute to the occurrence of stroke. Genetic factors for hypertension, Von Willebrand factors, Sickle cell disease among family may also contribute to increased risk of stroke. Risk of stroke further increases with a past history of stroke. Although heredity plays only a minor role in the pathogenesis of stroke, an increased risk is seen among first-degree relatives with a family history of stroke. The heredity factor when combined with unhealthy lifestyle leads to attenuated risk among the individuals.(35)(36)

Modifiable

- Cigarette smoking – It is one of the most important risk factor of stroke among young adults. Risk of stroke increases by four fold among young adults in smokers compared to non-smokers. The risk depends on both duration and dosage of exposure to smoking. Smoking more than 20 cigarettes per day are at higher risk of developing ischemic stroke. The risk of stroke increases by enhancing atherogenesis, triggering cardiac arrhythmias and arterial thrombosis and vasospasm. It also adds to the

economic burden in the family and country. If associated with other risk factors there will be synergistic effect on risk of stroke occurrence(37).

- Alcohol consumption–This is another modifiable and preventable risk factor for stroke in young adults. It differs among men and women. In men, binge drinking of alcohol are at higher risk of developing ischemic stroke than in non -alcoholics or alcoholic abstainers. Binge drinking has effect of raising blood pressure which further increases risk of stroke(38).In men, binge drinking is defined as six or more drinks (alcoholic beverage) in men, whereas it is four or more in women in one session. In women the risk increases with increase in intake of alcohol. Unlikely, consumption of wine has protective effect.

- Dyslipidaemia – Atherogenic dyslipidaemia is an independent risk factor of stroke among young adults and also plays a role in causing higher prevalence of recurrent stroke. Atherogenic dyslipidemia is defined as higher levels of low-density lipoprotein cholesterol (LDL-C) along with consideration of other factors such as high triglycerides (TGL) (TGL ≥150 mg/dL) and low high-density lipoprotein cholesterol (HDL-C) (HDL-C ≤40 mg/dL)(39).Elevated apolipoprotein B and A1 levels arealso associated with young stroke. Elevated LDL and TGL levels increase the intimal thickness of carotid artery thereby increasing atherosclerosis. It is associated with symptomatic intracranial stenosis identified by computed tomography (CT) imaging or magnetic resonance imaging of cerebral

blood vessels (MRI).They comprise a metabolic pattern that may be driven by insulin resistance, which ultimately leads to accelerated progression of atherosclerotic vascular disease(9).

- Abdominal obesity – defined as BMI more than 30kg/sq.m. Predisposing mechanism to stroke in obese individuals is likely due to its effect on arterial hypertension associated with elevated cholesterol levels. It mainly plays an important contributory factor for stroke. Upper body obesity is more important than lower body obesity as risk factor(40).Increased waist hip ratio is associated with early death. People should be encouraged to increase daily physical activity and reduction of weight in order to lessen the risk of stroke.Increased physical activity also decreases platelet aggregation and increase insulin sensitivity(41).
- Sedentary life style –It has been a contributory factor for occurrence of stroke in young individuals. Blood pressure, impaired glucose tolerance, insulin resistance are associated with altered lipid profile with increasing risk for stroke. Lifestsyle modifications like regular exercise, weight reduction measures and dietary modifications may help for good health and decrease in incidence.

- Hypertension – It is defined as systolic blood pressure (SBP) more than 140 mm Hg or diastolic blood pressure (DBP) more than 90 mmm Hg. It is considered both primary as well secondary cause of death among stroke

in young adults. 70% people with hypertension develop stroke. Hypertension increases stress and causes damage of vascular endothelium. This damage causes thrombi formation and ischemic lesions mainly affecting large extra-cranial vessels. Both elevated diastolic and systolic blood pressures are associated with increased concentrations of haemoglobin, which is a risk factor for ischaemic stroke(42)(43). Isolated systolic blood pressure and pulse pressures are at greater risk.

In chronic hypertension, there is vessel wall thickening and luminal narrowing which limit the capacity of the resistance vessels for dilation. In acute stroke, auto-regulation may be impaired in regions surrounding an acute lesion and even in the hemisphere contralateral to the lesion because of dilation of cerebral resistance vessels in an attempt to increase blood flow in response to tissue ischemia and acidosis. More recently, it has been shown that auto-regulation is impaired rapidly (dynamic auto-regulation) in conditions where systemic BP even is well preserved for controlled changes.About 10-20 mm of Hg decrease in SBP causes reduction of incidence of stroke of 28% in young adults(44).

- Diabetes mellitus: Increasing prevalence of diabetes causes increases macro-vascular complications thereby playing one of the major risk factor of concern in causing stroke. It is one of the long term complication of stroke(45). Three factors - fasting blood glucose (FBS), glycosylated haemoglobin (HbA1c) and duration of diabetes have significant impact on

risk of stroke among young adults. FBS more than 13.4mmol/l, HbA1c more than 6.5% and duration of diabetes for more than 7 years. Stroke occurring in diabetic individuals is usually no reversible. Persons with both type 1 and type 2 diabetes mellitus (DM) have increased susceptibility affecting both large and small vessel occlusive disease. Diabetes increases fibrinogen and clotting factors thereby causing increasing platelet aggregation promoting formation of arterial thrombosis(46). There is 11 times higher risk of stroke in young adults compared to older age group. Hyperglycemia does not present with signs typical of stroke whereas hypoglycaemia can mimic as stroke causing neurological deficits. It is therefore said that prompt treatment of hypoglycaemia in emergency conditions in suspicion of stroke.

- Oral contraceptives–risk of stroke in young women taking oral contraceptives is four times higher. High dose oestrogen doubles the risk of stroke than low dose oestrogen(47). Women with other associated factors like smoking, pro-thrombotic genetic variants and migraine, the risk increases further. High prevalence of thromboembolic stroke is seen in these conditions(48). Newer oral contraceptives with low levels of estrogen are being used to decrease the incidence of stroke in women.
- Pregnancy : Pregnancy and puerperium - Estrogen related stroke – Risk of stroke is high in third trimester and 6 weeks of post-partum period (49). Pre-eclampsia and eclampsia play a synergistic role of nine fold increase

in stroke occurrence(50). Amniotic fluid embolism, postpartum angiopathy and postpartum cardiomyopathy can result in cardio-embolism or infarction due to hypotension. It may also be influenced by underlying haemotological or thrombotic conditions

- Illicit drug abuse : Recreational drug abuse in young adults increases the susceptibility of stroke in young adults. Injectable drugs are more prone for embolic stroke(51). Use of certain drugs (eg, cocaine, amphetamines, crack) having sympathomimetic activity causing hypertension, platelet aggregation leading to endocarditis causing embolic stroke(52). Attimes, they may cause vasculitis of arteries and arterioles causing stroke. Drugs like heroin, opiates, cannabinoids also play a role in etiology of ischemic stroke.
- Migraine headache – There is increased risk of ischemic stroke among young women (35-45years) with migraine headache with aura (MA).The risk is attenuated with concomitant use of oral contraceptives, smoking and blood pressure. It has a bidirectional relation where cerebral ischemia may induce migraine headache(53). Most commonly they have occipital headaches involving nearly about one third of total cases. Special concern are people with patent foramen suffering with MA great high risk(54). There present guidelines indicate that early treatment and prevention of migraine headache in order to reduce the frequency of MA in women.

- Prior stroke or TIA – increasing mortality and DALY lost seen in young adults with recurrent stroke. It also has impact on emotional, social and physical condition of the individual causing increasing burden in family and also on country income.

ETIOLOGY:

- Atherosclerotic – thrombotic and cerebral embolic stroke are the predominant cause of AIS.

  Atherosclerosis: It mainly involves large vessels like both intra-cranial and extra-cranial arteries and small vessels (lacunar arteries)(55). It mainly begins with damage to the endothelial lining of vessel wall. The damaged area attracts platelets, calcium, fatty substances, fibrin and cellular debri which accumulate to form an atherosclerotic plaque. These plaque eventually increase in size and block the blood flow through the vessel thereby decreasing the blood supply leading to hypoxia.

These plaques become more vulnerable, when the lipid content increases in the plaque content within thin fibrous core.They become easily friable and get detached from the vessel form blood clots and flow easily in to the circulation and reach other areas and block the blood vessel(56). This denotes the second type of mechanism of stroke called cardio-embolic stroke. In both the mechanisms there will be vessel luminal stenosis as well as infiltration of vessel wall by inflammatory cells causing stiffness of vessel wall (57).

FIGURE 2:

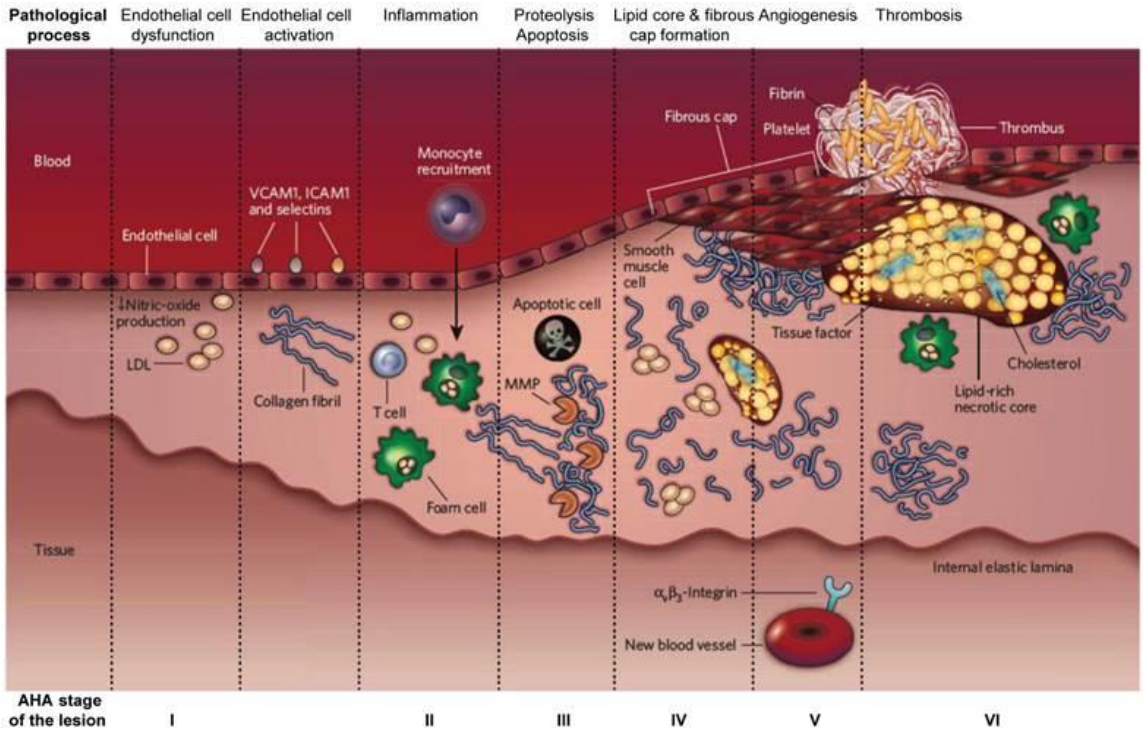
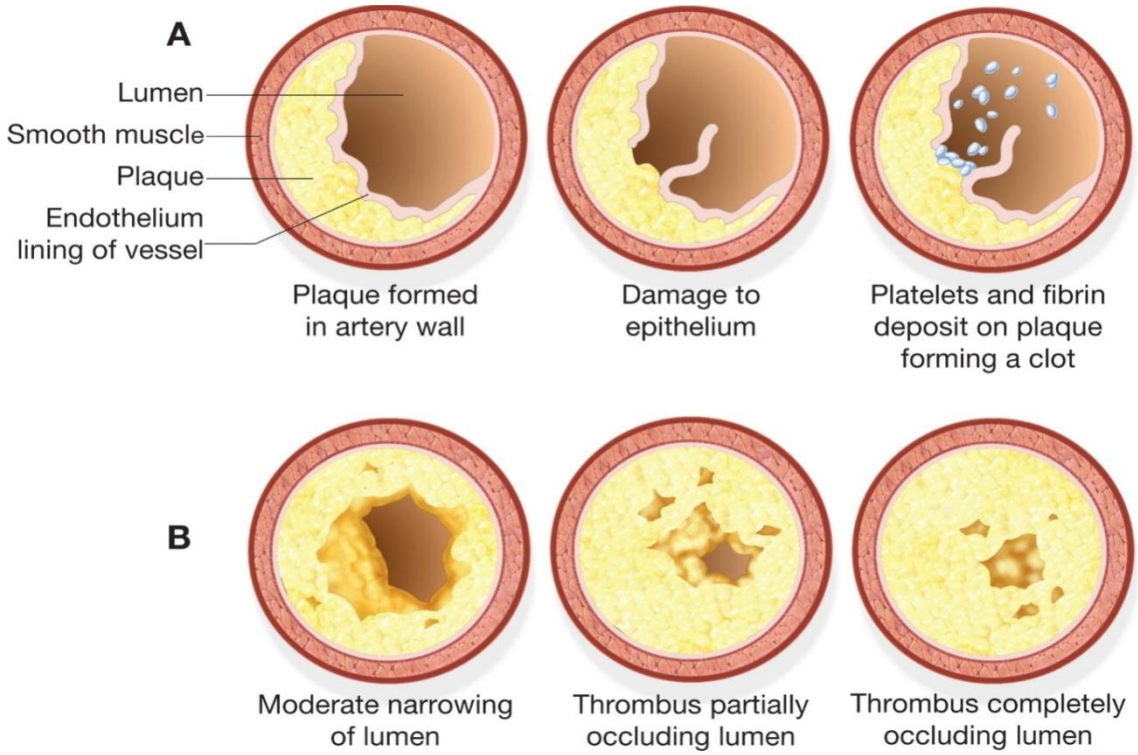


FIGURE 3:



Atheromatous plaques mostly form preferentially at branching points and curves of cerebral arteries. The most frequent sites involved are

- Internal carotid artery at its origin from the common carotid artery
- In the cervical part of vertebral arteries and at their junction to form basilar arteries
- In the stem or at the main bifurcation of middle cerebral arteries
- In the proximal posterior cerebral arteries as they wind around the midbrain
- In the proximal anterior cerebral arteries as they pass anteriorly and curve around corpus callosum.

The first three sites in the above mentioned are more frequent involved compared to cerebellar and ophthalmic arteries which are very less frequently involved.

- Large artery disease :

  Carotid and vertebral dissections - Defined as tear in intimal layer of vessel leading to blood flow in between the layers of vessel wall. The stasis of blood in between the vessel layers leads to formation of clot which can thromboembolise leading to stroke(58). It plays a role in causing stroke in young though it becomes a rare cause in older age group of stroke. Most commonly caused by trauma to blood vessel. It also causes haemorrhagic stroke in young adults. Spontaneous dissection is also seen

in few individuals. The predisposition for stroke increases if it is associated with connective tissue disorders.

- Lacunar infarct (Small artery disease) : Systemic hypertension and Migraine effect the small microvasculature causing lacunar infarcts in the individuals.
- Cardioembolism: It is the most common cause of arterial ischemic stroke (AIS) of all ages. It occurs very rapidly within seconds. The most common cause is atherosclerosis in older age group. It accounts of about one fifth of ischemic strokes(59). Whereas, this occurring in younger age group requires careful consideration as etiology varies comparatively. Most of the cases the emboli arises from a thrombus within heart. The arterial ischemic stroke caused by embolism from the heart can only be diagnosed, if at all there is an identifiable cardioembolic source which is the case in about 30% of ischemic stroke, by using transoesophageal echocardiography. It can provide the anatomic location of patients regarding the source of emboli.

Cardiac diseases – may be classified as congenital and acquired.

- Congenital heart disease is a one of major risk factor for cardio-embolic stroke especially in the perioperative period or following catheterization or extracorporeal membrane oxygenation (ECMO).
- Rheumatic heart disease (RHD) – it plays a significant role in causing stroke in young adults in developing countries. About 3-8% strokes are

attributed by RHD. It also plays a role in recurrent stroke. It remains as an occult cause where early identification and preventive measures must be taken to reduce the incidence and recurrence(60).

- Acquired conditions – this involves the most common cause of stroke. These commonly include Dilated cardiomyopathy (DCM), acute myocardial infarction (AMI), infective endocarditis (IE), Atrial Fibrillation (AF) and prosthetic valve placement. Coronary artery disease (CAD) share similar risk factors as that of stroke. left ventricular hypertrophy (LVH) and left atrial enlargement (LAE) further increases the relative risk of development of stroke(61).

- Elevated Homocysteine levels : Inborn errors of metabolism characterized by defect in methionine metabolism due to deficiency of enzyme cystathione b-synthase(CBS). Common pattern of inheritance is autosomal recessive. Deficiency of vitamin B12 and serum folate levels is another factor having contributory role. These enzyme and vitamin deficiencies causes increased accumulation of homocysteine levels in plasma and urine. This elevated homocysteine levels causes endothelial dysfunction affecting both small and large vessels causing thromboembolic events(62). It is mainly diagnosed by measuring the levels of homocysteine in urine and plasma. Most of them respond to vitamin supplements.

- Fibromuscular dysplasia – This condition mainly affects the medium sized vasculature mostly in young women of childbearing age group. It causes medial fibrosis of vessel wall with an unknown mechanism, predominantly involving the carotid vasculature(63). Stroke may be of thromboembolic or vascular stenosis may be the underlying cause. On angiography, this shows a typical beading pattern of involved vessel.
- Radiotherapy – Radiation received for head and neck malignancies are more prone to develop delayed onset of arterial ischemia stroke(64). Relative risk is doubled with radiotherapy.
- Haematological disorders :
  - Thrombophilia: It is mainly defined as a group of condition related to impairment of haemostatic mechanism which manifest as increased tendency to form thrombus. They may be classified as inheritable or acquired conditions. Deficiency in natural coagulants like protein C, protein S and antithrombin III deficiency, polymorphisms in activated protein C and disturbance of clotting mechanisms by mutation in prothrombin gene 20210G/A are classified under the inheritable causes. Among the inherited conditions, Factor V leiden and prothrombin 20210 mutation are most commonly associated with arterial ischemia stroke(AIS)(65).Among acquired conditions, Anti-phospholipid antibody syndrome (APLA) is most commonly associated with AIS. Acquired conditions are relatively at higher risk of causing stroke than inherited

conditions. People should undergo this workup with a background of prior episode suggestive of thromboembolic event or having a positive family history or recurrent pregnancy loss or no other identifiable risk factors(66). Screening among siblings and family members should be done for future prognostication.

- Myeloproliferative syndromes – They mainly include polycthemiavera (PV), myelofibrosis and essential thrombocythemia (ET). They are described to have high prothrombotic states which mainly occurs due to inflammatory insult to the vessel wall by host immune response towards malignant cells. About 60-70% constitute the arterial thrombosis. The risk of thrombosis even further increases because of the use of myelo-suppressive drugs(67). If associated with underlying valvular heart disease, there is a high risk of cardio-embolic stroke. ET affects microvasculature more.
- Sickle cell anaemia – Stroke in this condition is most fatal complication with unknown pathogenesis. Considered mechanism in the etiology of stroke in this diseased condition is that, the deformed sickle cells cause vaso-occlussion of vessels leading to stroke. Another mechanism is by hemolysis within the vasculature altering the endothelial structure of vessel wall(68). This condition mainly affects the large arteries.
- Vasculitides : Defined as occurrence of inflammation and formation of necrosis of vessel wall. It is classified as primary or secondary in nature.

Among the primary conditions Takayasu's arteritis, Polyarteritisnodosa (PAN), Wegener's granulomatosis (WG), Behcet's are more common conditions associated with stroke in young individuals. Another rare feature called primary angitis of central nervous system (CNS) which is a multifocal disorder considered as one of the etiology of stroke in young(69). In these conditions, there is inflammation of blood vessel wall which increases the thrombogenecity and alter the vessel tone predisposing to stroke. Secondary causes like infections, collagen vascular diseases predispose to stroke which were excluded in this study(70).

- Genetics: It may be single gene disorder or polygenic disorder or metabolic in nature.(TABLE 4)

TYPES:	GENE MUTATION	VESSEL AFFECTED
CADASIL	Notch 3 receptor	Small vessel disease
CARASIL	Notch 3 receptor	Small vessel disease
Fabry disease (X-linked recessive)	α-galactosidase A	Large and small vessel disease
MELAS (maternal)	Transfer RNA	Complex
Marfan syndrome (autosomal dominant)	Fibrillin 1	Cardioembolism and arterial dissection
Ehlers–Danlos syndrome (autosomal dominant) – type IV	Collagen type III	

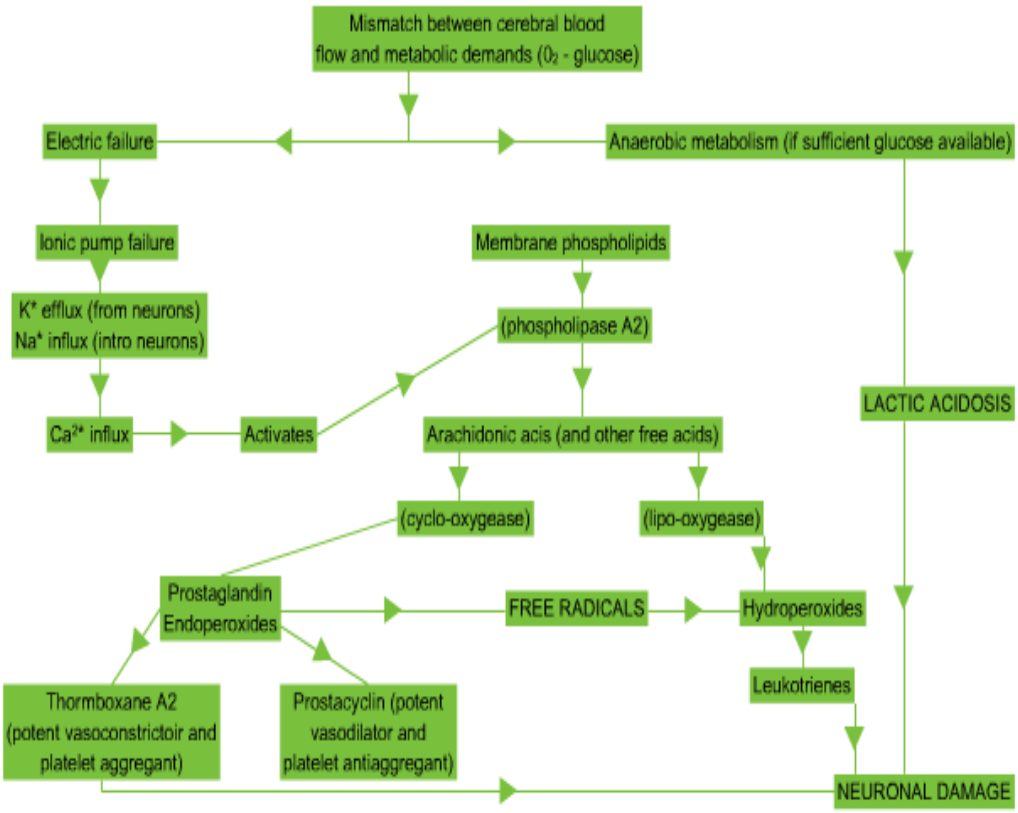
- CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)- mutation causes progressive degeneration of smooth muscle cells in vessel wall causing stroke in late childhood or early adulthood(71). High risk for recurrent stroke in young. It is identified by classical MRI changes which shows bilateral temporal pole hyperintensity – punctate and nodular lesions.
- CARASIL(cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy) – autosomally recessively inherited CADASIL associated with acute features of lumbago, spondylosis deformans, diffuse baldness and progressive mental and motor deterioration. Most common age of onset is 25-30years of age (younger age comparatively to CADASIL). On imaging , it is typically identified as diffuse and homogenous lesions.
- MELAs – mitochondrial myopathy, encephalopathy, lacto-acidosis and stroke. It is a multisystemicmaternally inherited disorder which are characterised by stroke like episodes(72). In this condition mostly posterior regions like temporo-parietal and occipital regions are involved. Due to mitochondrial dysfunction, nitric oxide metabolism is impaired and free radicals are released which cause impairment of auto-regulation. Cardiomyopathy due to mitochondrial disease may cause cardio-embolic stroke. They are transient in nature and reflected

in abnormalities on neuroimaging(73). Muscle biopsy helps in diagnosing, by identifying the abnormal proliferation of mitochondria.

- Fabry's disease – X-linked genetic disorder where there is accumulation of lysosomes in vascular endothelium leading to narrowing of the vessels and infarction in affected young adult males(74). It involves brain, kidney, heart and skin. About 25% of individuals with fabry's disease develop stroke involving both carotid and vertebrobasilar regions(75). Alpha galactosidase replacement decreased the incidence of cerebrovascular incidents.
- Heritable disorders of connective tissue – This mainly involves the mutation in collagen and elastin which mainly constitute the main content of the vessel wall. Of the disorders affecting collagen fibres, Ehlers Danlos syndromes (EDS), osteogenenis imperfect (OI), autosomal dominant polycystic kidney disease (ADPKD) and collagen type IV related small vessel disease are most commonly associated with stroke(76). These are associated with formation of aneurysms in the vessel wall and are complicated with carotid and vertebral artery dissections. Among those affecting the elastin content of vessel wall, Marfan's syndrome, LoeyzDietz syndrome (LDS type I and II) and pseudoxanthoma elasticum are commonly associated with occurrence of stroke in young.

- Amyloid angiopathy: It is associated with amyloid deposition in leptomeningeal walls and cerebral arteries and arterioles. Most commonly involves the occipital region and considered severe if it involves the same region. Mostly it causes haemorrhagic stroke.
- Moyamoya disease : it is a genetic disorder with AD pattern of inheritance characterised by thickening of intimal carotid vessels. It has bimodal age pattern at age of 5 years and 30-50years of age(77). It mainly causes ischemic stroke in younger age group whereas associated with haemorrhagic stroke in adults.

PATHOPHYSIOLOGY OF STROKE (FIGURE 4):



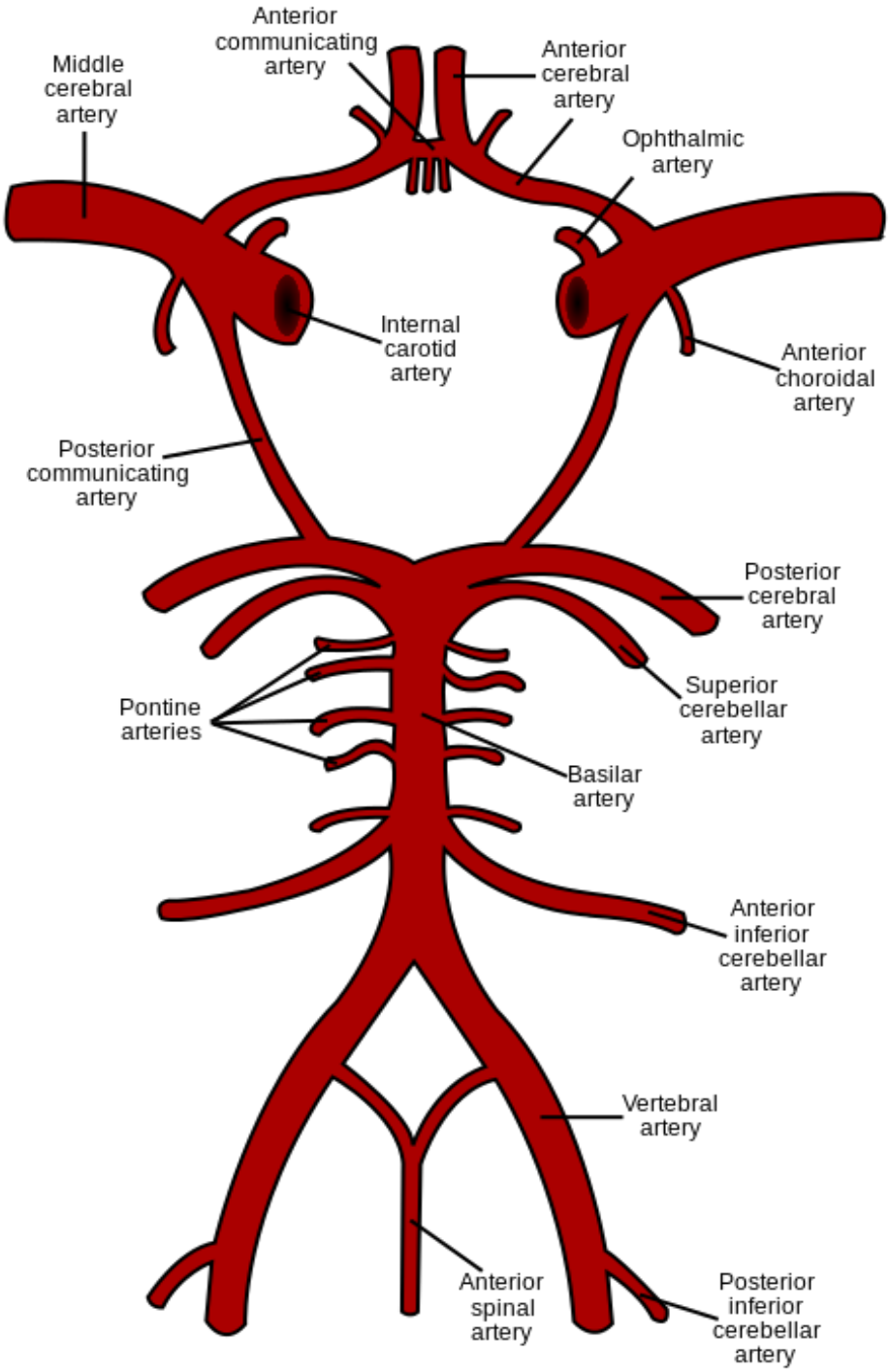
ANATOMY AND CLINICAL MANIFESTATIONS

o ANATOMY OF CEREBRAL CIRCULATION:

Brain is the highest perfused organ in the body. It receives about 20% of total circulation and also have maximum consumption of oxygen in the blood. It is mainly supplied by two pairs of large arteries – internal carotid arteries and vertebral arteries(78).

Internal carotid artery supply about $3/5^{th}$ of cerebrum.The two vertebral arteries join together to form basilar artery which supplies cerebellum and brain stem. These two arterial circulation join together with the help of communicating branches to form circle of willis (COW)(79)(55). (FIGURE 5)

FIGURE 5:


Anterior communicating artery
Middle cerebral artery
Anterior cerebral artery
Ophthalmic artery
Internal carotid artery
Anterior choroidal artery
Posterior communicating artery
Posterior cerebral artery
Superior cerebellar artery
Pontine arteries
Basilar artery
Anterior inferior cerebellar artery
Vertebral artery
Anterior spinal artery
Posterior inferior cerebellar artery

- The internal carotid group produce three main vessel branches which include –

1. Ophthalmic artery – supplies the meninges, contents of orbit.
2. Anterior cerebral artery (ACA) – these are pair of arteries supplying the medial portions of frontal lobes along with prefrontal and supplementary motor cortex and superior medial parietal lobes. They are further subclassified into 5 smaller branches called callosal arteries as they also supply the carpus callosum. Due to collateral supply by anterior communicating artery, stroke due to ACA is very rare.

- Clinical relevance –
    - Occlusion of ACA may cause following symptoms:
    - Contralateral lower limb upper motor neuron type (UMN) of weakness
    - Contralateral sensory loss in lower limb
    - Due to frontal lobe involvement – Behavioural abnormalities, cortical release reflexes – grasp reflex, sucking reflex, gegenhalten phenomenon.
    - Transcortical aphasia.

3. Middle cerebral artery (MCA) – It also a paired artery which supplies anterior temporal and insular cortices. They are connected to ACA with the help of anterior communicating branches and connected with PCA with the help of posterior communicating branches. They are

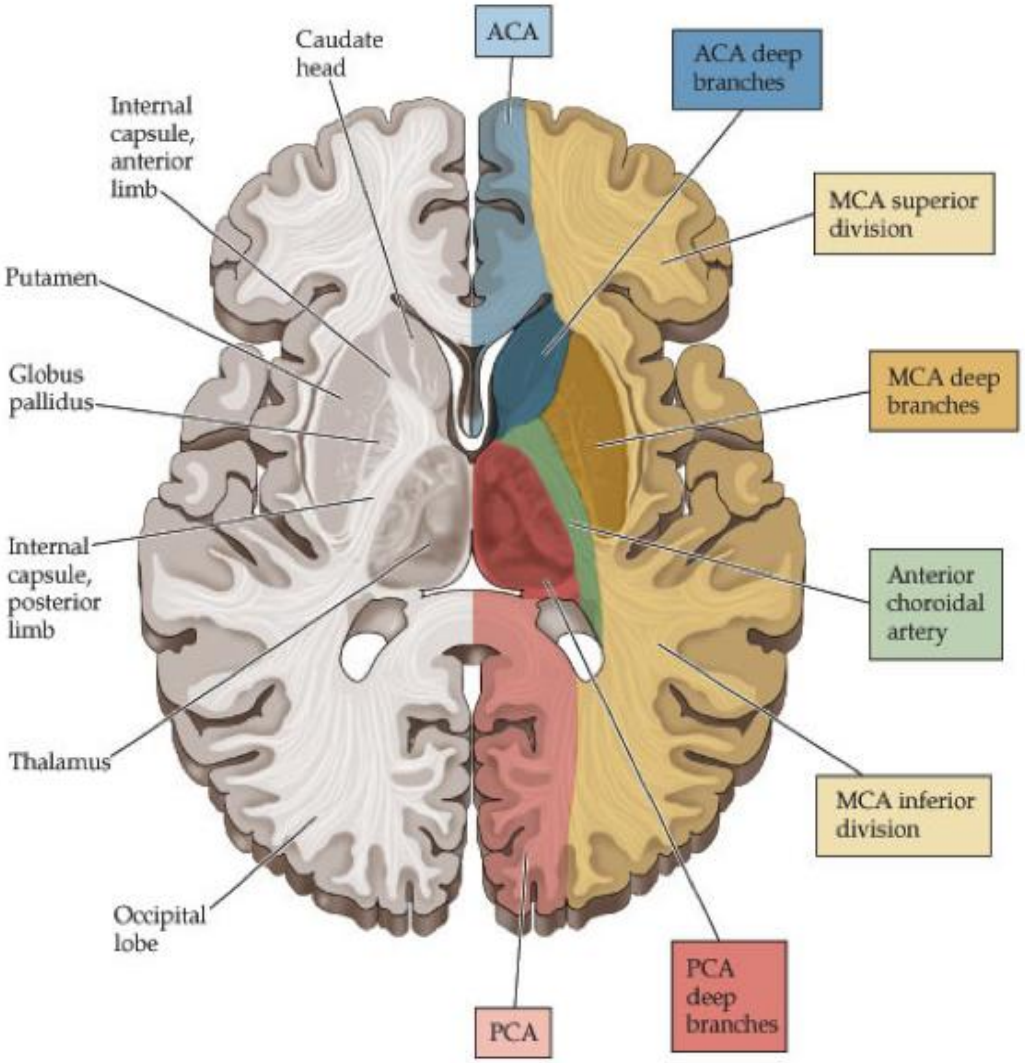
further divided into 4 parts or segments in their course of supply. They supply the bulk of lateral surface of the hemispheres along with speech areas (Broca's and Wernicke's areas)

- Clinical relevance –
  - Contralateral upper and lower limb UMN type of paralysis
  - Contralateral sensory loss over face and arm
  - If lenticulostriate branches of MCA are involved –
    - If involvement of dominant hemisphere → aphasia
    - Involvement of non-dominant hemisphere → contralateral neglect syndrome

4. Posterior cerebral artery (PCA) – it is one of the paired arteries which supply the posterior part of the brain which includes occipital lobe. It is divided into 2 branches – cortical and ganglionic vessels.

- Clinical relevance –
  - Contralateral loss of pain and temperature
  - Contralateral homonymous hemianopia with macular sparing
  - Alexia and agraphia
  - Weber's syndrome – third cranial nerve palsy with contralateral hemiplegia
  - Horner's syndrome

FIGURE 6:


Caudate head
ACA
ACA deep branches
Internal capsule, anterior limb
MCA superior division
Putamen
Globus pallidus
MCA deep branches
Internal capsule, posterior limb
Anterior choroidal artery
Thalamus
MCA inferior division
Occipital lobe
PCA deep branches
PCA

MANAGEMENT:

NON INVASIVE METHODS:

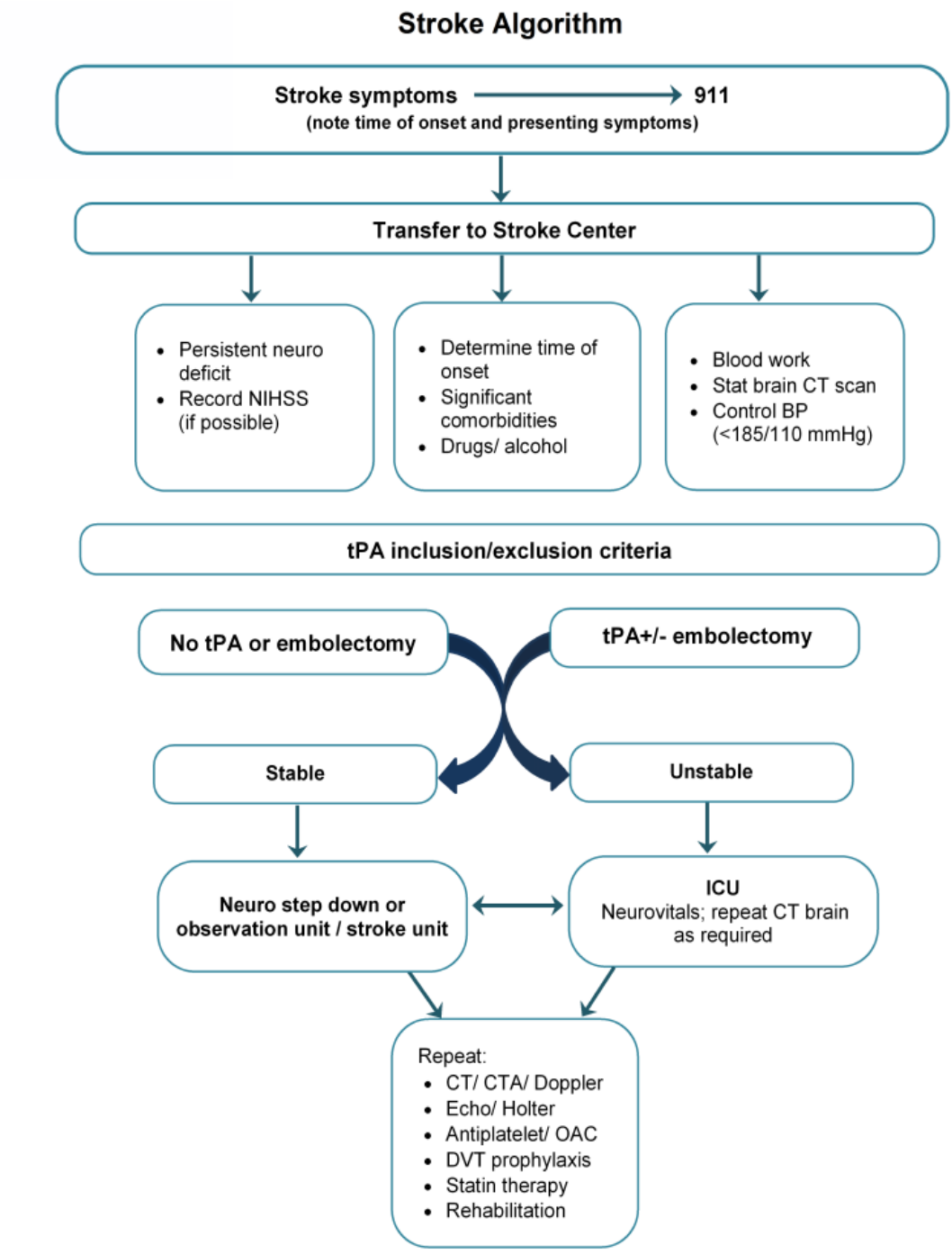
Patients with AIS, diagnosing stroke at early hand plays a key role in many ways:

- ✓ To study the anatomical vasculature supplying the brain and also to determine the possible mechanism associated with occurrence of AIS.
- ✓ To know the possible etiological association causing stroke in young adults.
- ✓ In assessment of the clinical outcome and prognostication of the condition.
- ✓ It helps for further management – mainly in the ED, where it plays a crucial role for diagnosis of AIS in order to decide about further management.

Therefore, a standard approach for diagnosis and treatment for stroke in young adults must be established in a primary health care centres and standard educational institutions for management of stroke in emergency.

DIAGNOSIS: Detailed clinical history from the patient or reliable attenders and rapid clinical examination plays a diligent role in diagnosis of AIS in ED.

FIGURE 7:



NIHSS: The National Institutes of Health Stroke Scale; **tPA:** Tissue plasminogen activator; **ICU:** Intensive care unit; **CT:** Computed tomography; **CTA:** Computed tomography angiography; **OAC:** Oral anticoagulant; **DVT:** Deep vein thrombosis

It also helps in assessing the arterial territory involved and area of brain affected by examining clinically.

Stroke scoring systems : Rapid assessment with the help scoring systems is needed in the patients with suspicion of stroke. several scoring scales are mainly used to assess the baseline characteristics for treatment outcome (80). In this study, clinical assessment by NIHSS scoring scale is used in the ED (used in this study) to know the severity of stroke at onset in young adults and used for prognosis and assess clinical outcome among them. These scales mainly help in improving accuracy of diagnosis of AIS and also help in determining the appropriate treatment and calculated outcome. No single scale will be able to assess all the effects of stroke that means not all parameters of stroke can be assessed completely by these scales. Several scoring scales are being designed and standardized, used varying on institutional presentation.

Early imaging of brain either CT or MRI with or without angiography has to be done in the ED presented with suspicion of stroke. By doing this, haemorrhagic stroke is ruled out where the line of management differs from that of AIS.

Routine baseline investigations to be done are (TABLE 5):

Complete haemogram	
Blood sugars	Hypo or hyper glycemia
Urine routine	Diabetes , infection
Serum electrolytes	Hyponatremia or hypokalaemia or hyperkalaemia
Renal function tests	Renal failure
Fasting lipids	Dyslipidemia
Homocysteine levels	Homocystinemia
Serology	Vasculitis , Infections, HIV, VDRL
ECG	Left ventricular hypertrophy (LVH), Atrial fibrillation, arrhythmias, AMI
Echocardiography	Infective endocarditis, atrial myxoma
ESR, CRP	Autoimmune causes-vasculitis, SLE
To do :	
ANA profile, APLA	APLA syndrome, SLE, vasculitis
Coagulation profile	Protein C and S deficiency, anti thrombin III deficiency, hyperfibrinogenemia.
Genetic studies (optional)	CADASIL, MELAS, CARASIL.,etc

TREATMENT:

Treatment is mainly aimed to reverse the hypoxic brain injury or lessen further damage of brain from hypoxia caused by decreased blood supply due to occlusion of the blood vessels supplying the brain.

At the presentation to ED with acute stroke, the primary management is to assess the airway, breathing and circulation initially(81). Then treat the hypoglycaemia(<60mg/dl) on presentation identified as it may act as one of the stroke mimic.Hyperglycemia has poor outcomes of stroke. Hence, early treatment is needed.

Blood pressure : Our goal is to reduce the blood pressure by 15% of initial presentation within 24hrs of onset provided if SBP > 220 mm Hg and DBP >120 mm Hg for AIS.

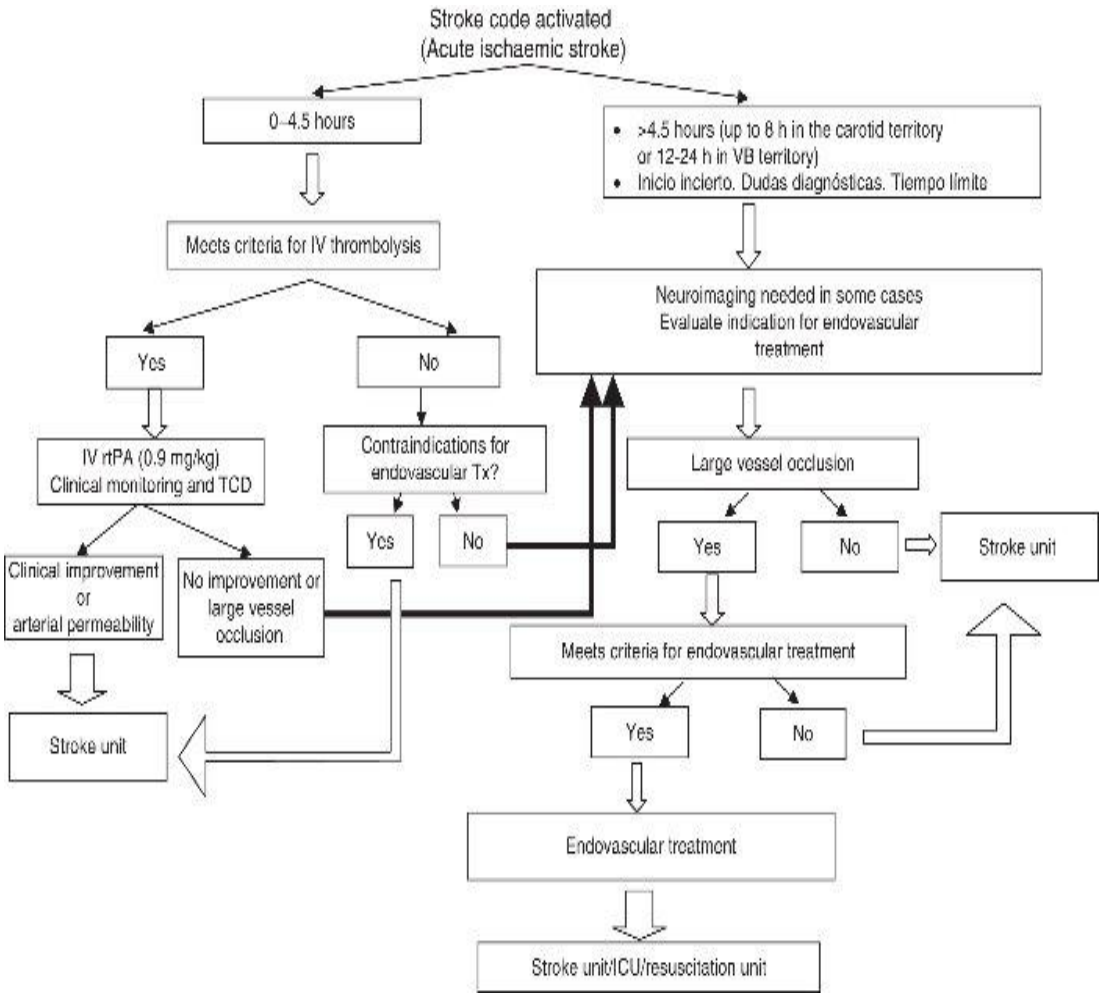
❖ ***Early fibrinolysis :***

According to AHA/ASA guidelines for the management of AIS, it is indicated to thrombolyse patient with fibrinolytics in order to restore the blood flow to the brain and early resolution or neurological deficits. For this purpose, most commonly used fibrinolytic drug is r-tPA (recombinant tissue plasminogen activator). Streptokinase which has a major role in AMI, has high incidence of complications in acute AIS. Hence this drug is of not on regular use for AIS. Individual presented to ED must be identified by inclusion and exclusion criteria where patient is a feasible candidate for fibrinolysis(82). They must be

thrombolysed within a window period of maximum of 4.5hrs from the onset of symptoms.

According to National institute of Neurological Disorders and Stroke (NINDS) and several other trials(83), the benefit of receiving t-PA is, no increased mortality and excellent recovery , outcomes the incidence of occurrence of intracerebral haemorrhage among receiving with t-PA.

FIGURE 8:



CRITERIA FOR THROMBOLYSIS IN AIS:

INCLUSION CRITERIA:

- ✓ Onset of symptoms <3 hours before beginning treatment (Onset time is defined as either the witnessed onset of symptoms or the time last known normal)
- ✓ Age ≥18 years
- ✓ Informed consent - Potential risks and benefits of IV t-PA treatment discussed with patient and/or family members and they have verbalized understanding (to be documented in patient's record). If patient unable to give verbal consent and no family available, IV t-PA can be given under Emergency Doctrine. Written informed consent not required for IV tPA when given within 3 hours of symptom onset.

ABSOLUTE EXCLUSION CRITERIA

- ✓ Significant head trauma or prior stroke in previous 3 months
- ✓ Symptoms suggestive of any history of haemorrhage stroke
- ✓ Intracranial neoplasm, arteriovenous malformation, or aneurysm
- ✓ Recent intracranial or intra-spinal surgery
- ✓ Elevated blood pressure (systolic >185 mm Hg or diastolic >110 mm Hg)
- ✓ Active internal bleeding
- ✓ Blood glucose concentration <50mg/dl (2.7mmol/L)
- ✓ Acute bleeding diathesis, including but not limited to: Platelet count <1,00,000/mm^3 (In patients without history of thrombocytopenia,

treatment with IV rtPA can be initiated before availability of platelet count but should be discontinued if platelet count is <100 000/mm³.)

- ✓ Heparin received within 48 hours, resulting in abnormally elevated aPTT greater than the upper limit of normal
- ✓ Current use of anticoagulant with INR >1.7 or PT >15 seconds and current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT; TT; or appropriate factor Xa activity assays)
- ✓ CT demonstrates multilobar infarction (hypodensity>1/3 cerebral hemisphere)

RELATIVE EXCLUSION CRITERIA :

- ✓ Only minor or rapidly improving stroke symptoms (clearing spontaneously)
- ✓ Seizure at onset with postictal residual neurological impairments
- ✓ Major surgery or serious trauma within previous 14 days
- ✓ Recent gastrointestinal or urinary tract haemorrhage (within previous 21 days)
- ✓ Pregnancy

To extend IV tPA to 4.5 hours from symptom onset/last known normal, the following additional criteria MUST be met:

- ✓ Patient is < 80 years of age

- ✓ Patient does not have a history of both diabetes AND stroke
- ✓ Patient is not taking Warfarin (Coumadin) or any other anticoagulant regardless of INR/coagulation results
- ✓ NIHSS is < 25
- ✓ Written informed consent obtained from patient and/or family – required when IV tPA given within the 3-4.5 hour window.

❖ ***Anti coagulants:***

Anticoagulation is not recommended in all the patients with AIS in emergency condition. Drugs most commonly use are low molecular weight heparin (LMWH) or unfractionated heparin (UFH)(84). They are generally used to prevent venous thromboembolism. But later recommendations suggest as of only with following specified clinical situations, anticoagulation therapy is indicated :

- Conditions with potential high risk ofearly cardiogenic reembolization
- Symptomatic dissection of arteries supplying the brain
- Symptomatic extra-cranial or intra-cranial atherosclerotic stenosis
- Basilar artery occlusion before or after intra-arterial pharmacological or mechanical thrombolysis
- Known hypercoagulable states
- Cerebral venous sinus thrombosis

❖ ***Anti-thrombotic agents :***

They are mainly used for secondary prevention of stroke. Drugs most commonly used are aspirin. Clopidogrel and extender release dipyridamole. Newer antiplatelets dabigatran, apixaban and rivaroxabanrae being studied for anticoagulation comparing with warfarin for primary end point (84). According to guidelines, aspirin should be given within 24 to 48hrs of onset of stroke to prevent mortality and primary end point.

Endovascular techniques – intra-arterial fibrinolysis, thrombo-embolectomy, suction thrombectomy, angioplasty and revascularisation are few among known endovascular procedures. The main aim of these is to recanalise the thrombosed vessel to improve the blood flow. For this a team of skilled neurologists, interventional radiologists, anaesthesiology, nursing and technical support for optimal success.

- ***Neuro protection:***

Several novel neuro-protective agents like citicholine, traxoprodil, ONO-2506, magnesium, DP-b99 and NXY-059 have been identified. They limit the infarct size and improve functional outcome (primary end point)(85). They act as free radicals scavengers and inhibit further occurrence of neuronal cell death.

❖ ***Rehabilitation centres :***

The main aim of these centres is to improve the quality of life of stroke survivor by improving the skills to do the daily day to day activities. A team of neurologist, psychiatrist, occupational therapist, speech language therapists, dietician and social workers play an important role in achieving the desired result(86).

RESULTS

In this study, about 50 consecutive cases admitted with AIS, which met inclusion and exclusion criteria are taken into the study. At presentation, along with complete history taking, relevant clinical examination, scoring was done, based on NIHSS and mRS scale in ED. The risk factors, etiology and clinical outcome were analysed in this study.

GENDER:

Among the study population of 50 patients, 36 (72 %) were males and 14 (28 %) were females suffered with AIS.

FIGURE 9:

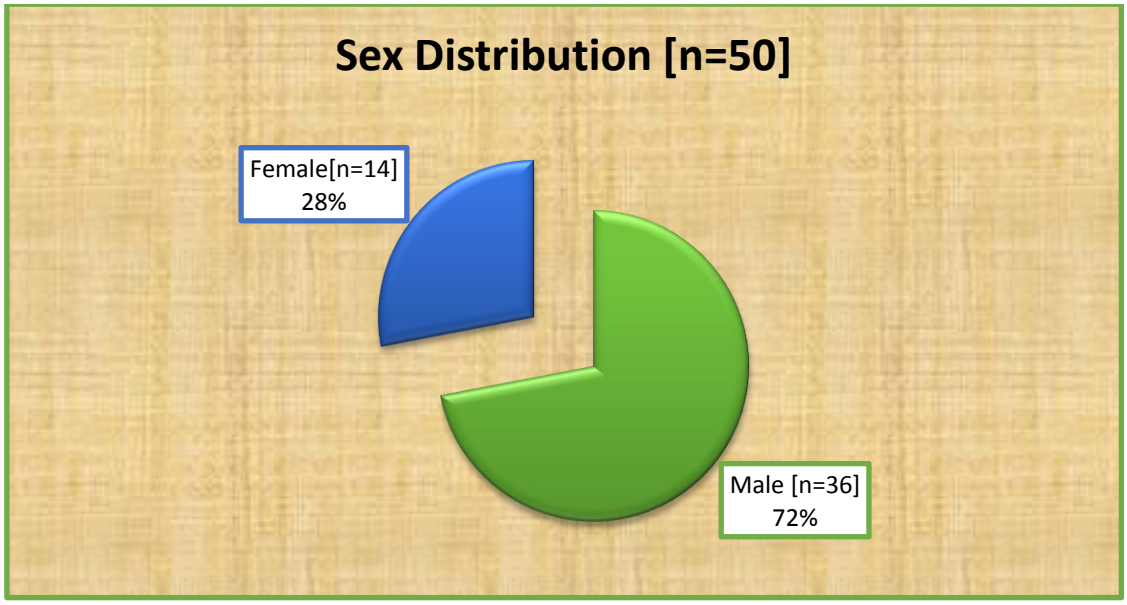


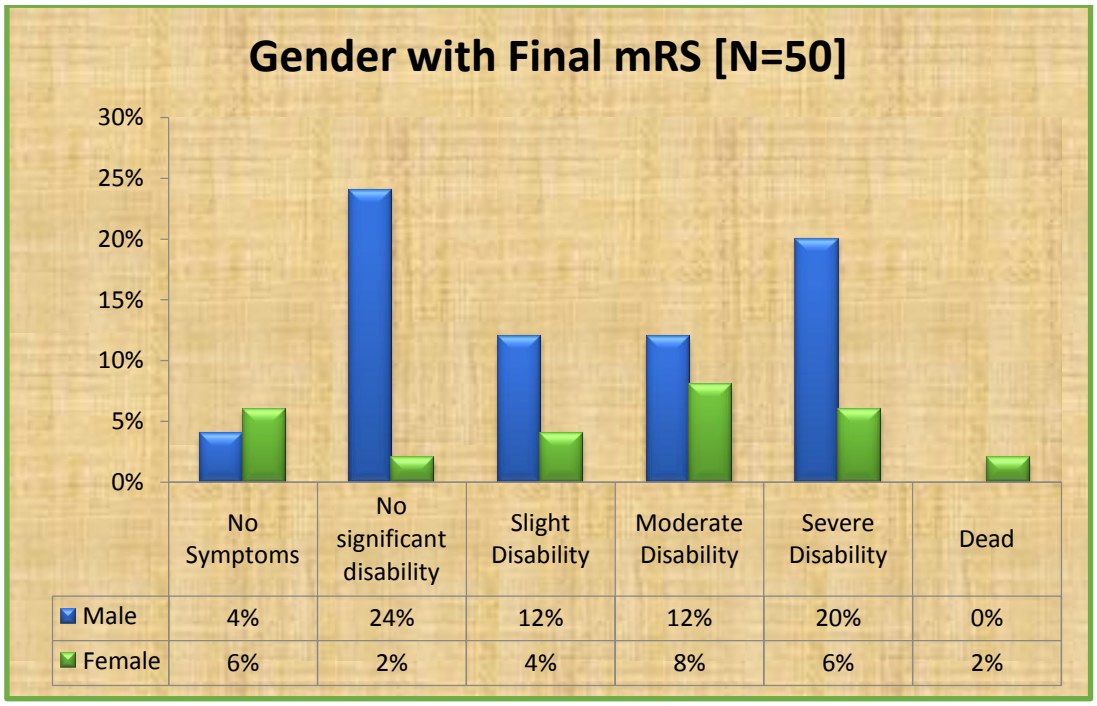
TABLE 6:

Gender with Final mRS score							
	FINAL mRS SCORE						
Gender	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
Male	2	12	6	6	10	0	36
Female	3	1	2	4	3	1	14
Total	5	13	8	10	13	1	50

Out of 36 males in the study, 10 had persistent severe disability and with 6 each having mild to moderate disability and 2 have recovered completely from disability and symptoms. Among them, 2 had been death as final consequence.

Among 14 females in the study, 3 had severe disability and 3 had recovered completely from the symptoms. Rest all were between of having mild to moderate disability. Only one among the female population had death as final consequence in the study.

FIGURE 10:



Out of 50 patients, death occurred in about 3 patients. Among the females, death occurred among 1 patient accounting to mortality of 2%, whereas among males, 2 deaths out of 36 patients accounting to 2% of mortality.

AGE:

Among the age groups involved, most commonly patients were between 41-45 years of age group constituting of 50% of total patients constituting if about 25 patients. Out of which 19 were males and 6 females.

(TABLE 7)

Age Distribution

	SEX			
Age	Male	Female	Total	(%)
< 30	2	1	3	6%
31 - 35	1	5	6	12%
36 - 40	14	2	16	32%
41 - 45	19	6	25	50%
Total	36	14	50	100%

Between 36-40 years age group, constituted of about 32%(16 patients) of total study population. Out of which, 14(28%) were males and 2(4 %) were females. 6 patients with AIS (about 12%) were categorised under age group of 31-35years, out of which 1(2%) was male and 5(10%) were females. And about 3 patients, which is of about 6% of total study population fall under 30years of age group, among which 2(4%) were males and 1 (2 %) was female.

(FIGURE 11):

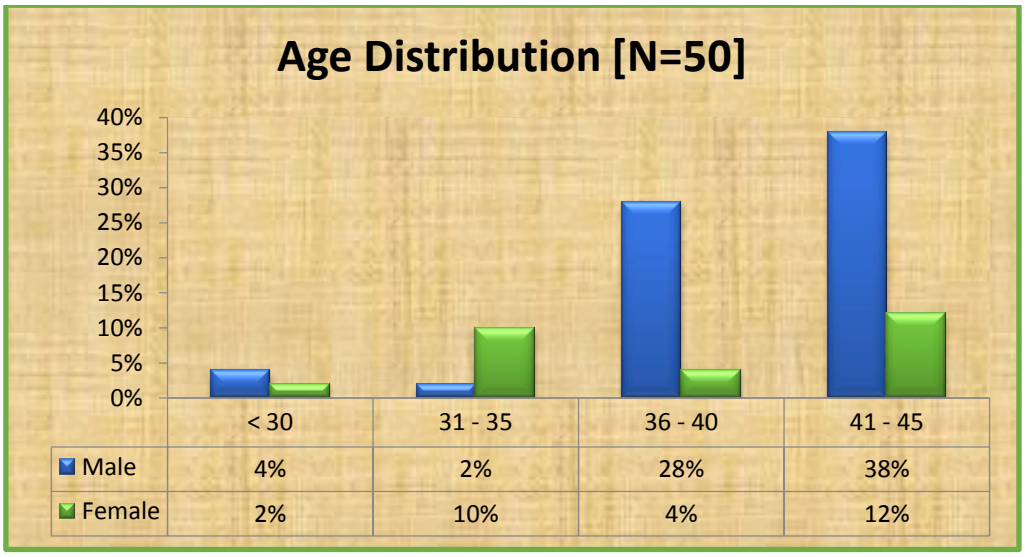

Age Distribution [N=50]
40%
35%
30%
25%
20%
15%
10%
5%
0%
< 30
31 - 35
36 - 40
41 - 45
Male
4%
2%
28%
38%
Female
2%
10%
4%
12%

TABLE 8:

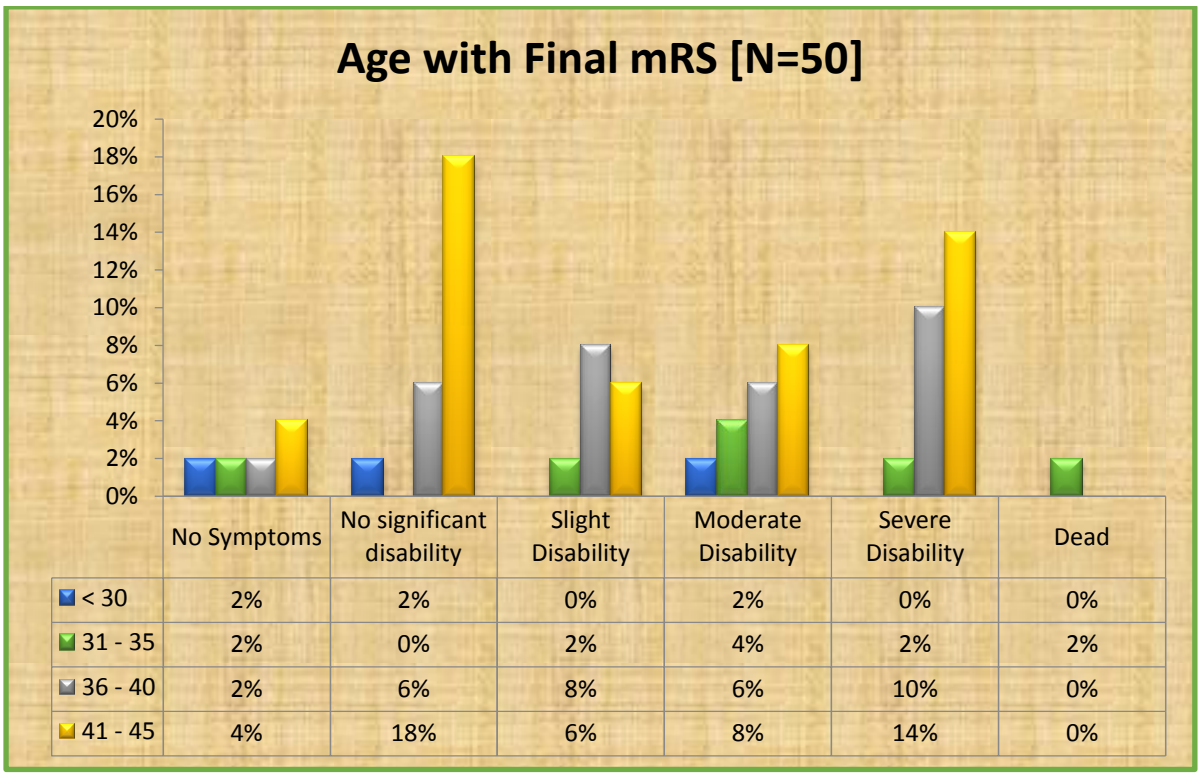
Age with Final mRS score							
	FINAL mRS SCORE						
Age	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
< 30	1	1	0	1	0	0	3
31 - 35	1	0	1	2	1	1	6
36 - 40	1	3	4	3	5	0	16
41 - 45	2	9	3	4	7	0	25
Total	5	13	8	10	13	1	50

When correlating with final outcome with respect to age group of study population, 13 patients had persisting severe disability, out of which 7 were among the age group 41-45years, 5 were in between 36-40years and 1 was between 31-35years. 10 patients had moderate disability depending the ranking scale, 4 were under 41-45years, 3 were in between 36-40, 2 were among 31-35 years of age group and 1 was less than 30years of age.

Among them, about 13 patients had complete recovery from clinical signs left with no disability and were able to carry out their regular activities with ease. Among them, 9 were under 41-45years of age group. About 5 patients had complete recovery of both signs and symptoms, among which 2 are under 41-45 years of age group and rest of them 1 each among each category of age respectively.

Death occurred among three patients in total study, 1 each which fall under the age groups of 41-45 years , 36-40years and 31-35 years category.

FIGURE 12:



	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead
< 30	2%	2%	0%	2%	0%	0%
31 - 35	2%	0%	2%	4%	2%	2%
36 - 40	2%	6%	8%	6%	10%	0%
41 - 45	4%	18%	6%	8%	14%	0%

Risk factors:

Among 50 patients observed, 29 were smokers, 3 chewed tobacco, 26 consumed alcohol. Among them, 24 patients had dyslipidemia, 13 had hyperrtension, 13 diabetes and only 7had heart disease. Out of 50, 5 had recurrent episode of stroke and about 3 patients have been observed to have no associated risk factors. Other associated risk factorswhich constitute trauma, thyroid disorder, renal failure and bleeding disorders were observed in the study population.

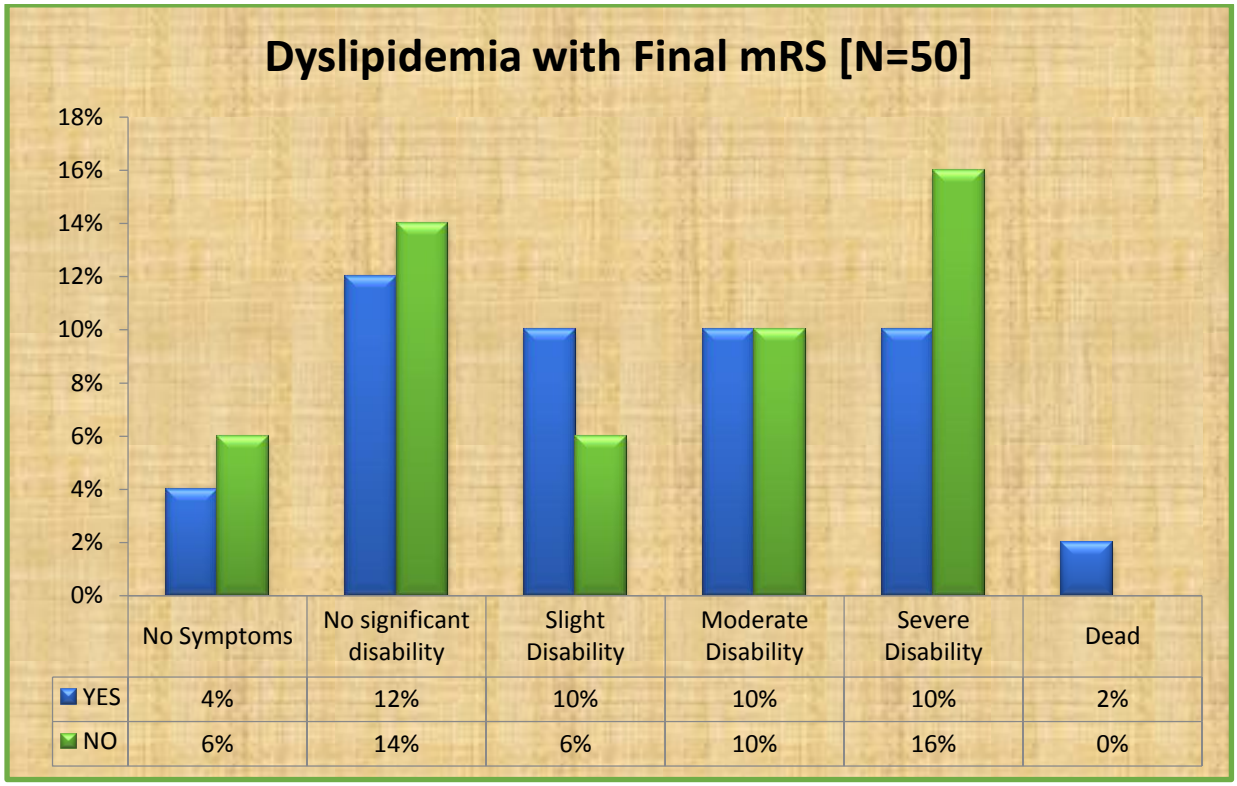
DYSLIPIDEMIA:

TABLE 9:

DYSLIPIDEMIA with Final mRS score							
	FINAL mRS SCORE						
DLP	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
YES	2	6	5	5	5	1	24
NO	3	7	3	5	8	0	26
Total	5	13	8	10	13	1	50

Out of 50 patients, 24 patients had history of dyslipidemia. Among them with dyslipidemia, 1 patient got expired, 5 patients were left with persistent severe disability, 5 were with moderate and slight disability respectively. 8 were left with no disability and completely recovered from AIS. Patients who had no history of dyslipidemia, constituted about 26 patients of total population. Among them, 8 patients were left with severe disability, 5 patients had moderate disability, 3 patients had mild disability. 10 patients had recovery with no disability.

FIGURE 13:


Dyslipidemia with Final mRS [N=50]
18%
16%
14%
12%
10%
8%
6%
4%
2%
0%
No Symptoms
No significant disability
Slight Disability
Moderate Disability
Severe Disability
Dead
YES 4% 12% 10% 10% 10% 2%
NO 6% 14% 6% 10% 16% 0%

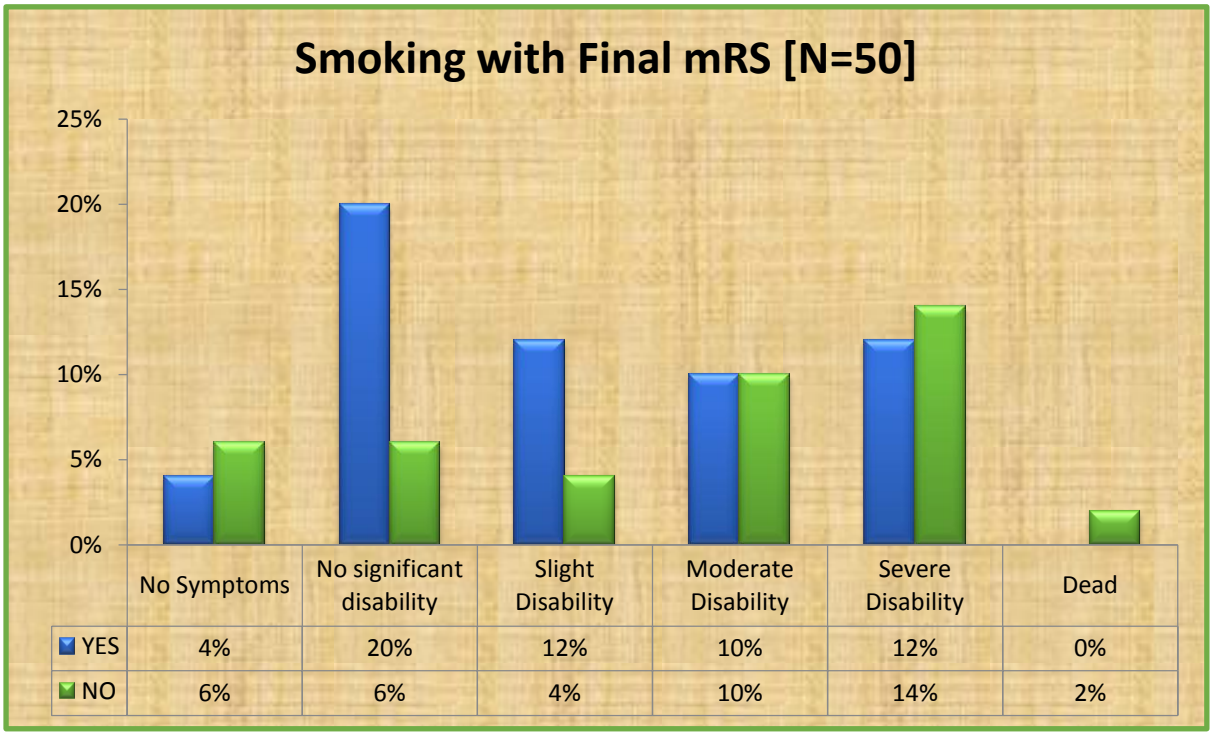
SMOKING:

TABLE 10:

Smoking with Final mRS score							
	FINAL mRS SCORE						
Smoker	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
YES	2	10	6	5	6	0	29
NO	3	3	2	5	7	1	21
Total	5	13	8	10	13	1	50

Among 50 patients of study population, 29 patients were smokers ad 21 patients were non smokers. Among the smokers, 6patients had severe disability. 5 patients and 6 patients had moderate to slight disability respectively. Total of 12 patients had no disability, out of which 2 patients recovered completely without signs and symptoms. Among the non-smokers, 1 patient had death and 7 patients had severe disability.5 patients and 2 patients had moderate and slight disability respectively. 6 patients total have recovered clinically, out of which 3 had complete recovery from both signs and symptoms.

FIGURE 14:


Smoking with Final mRS [N=50]
25%
20%
15%
10%
5%
0%
No Symptoms
No significant disability
Slight Disability
Moderate Disability
Severe Disability
Dead
YES
4%
20%
12%
10%
12%
0%
NO
6%
6%
4%
10%
14%
2%

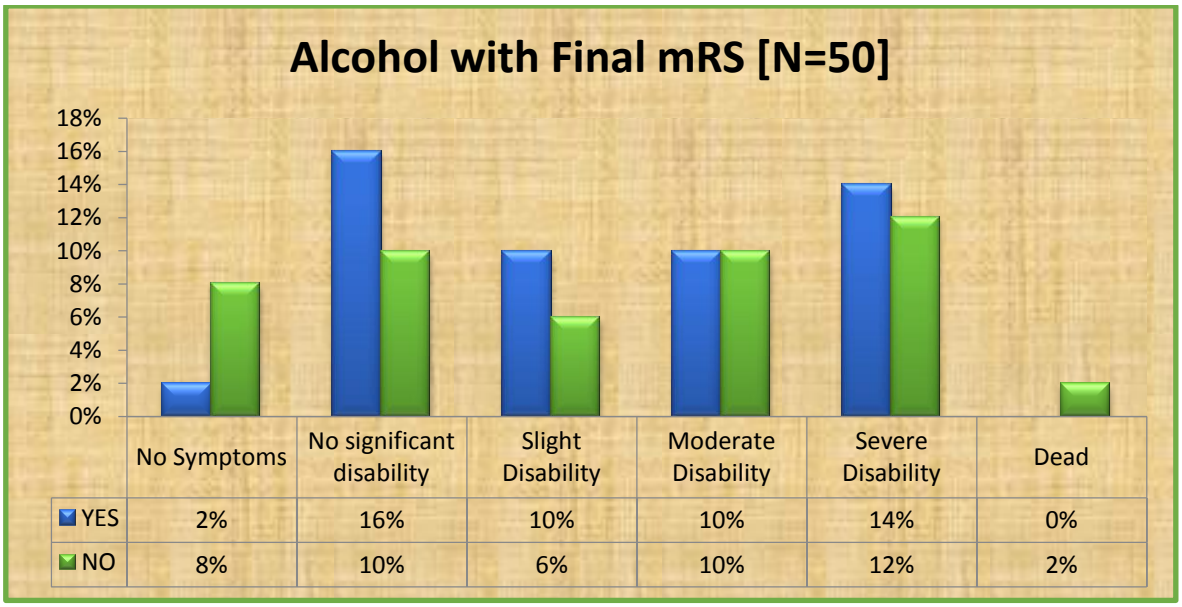
ALCOHOL:

TABLE 11:

Alcohol with Final mRS score							
	FINAL mRS SCORE						
Alcohol	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
YES	1	8	5	5	7	0	26
NO	4	5	3	5	6	1	24
Total	5	13	8	10	13	1	50

Among the 50 patients, 26 patients were alcoholic and 24 patients were non-alcoholic. Out of 26 patients of alcoholics, 7 patients had severe disability. 5 patients each had moderate and slight disability respectively. 9 patients in total had complete recovery clinically, among which only had complete recovery from both signs and symptoms of stroke. Among the non-alcoholics, 1 had experienced death as final outcome. 6 patients had severe disability. 5 patients and 3 patients had moderate and slight disability respectively. 9 patients had complete recovery clinically, among which 4 had recovery completely from both signs and symptoms of stroke.

FIGURE 15:



DIABETES:

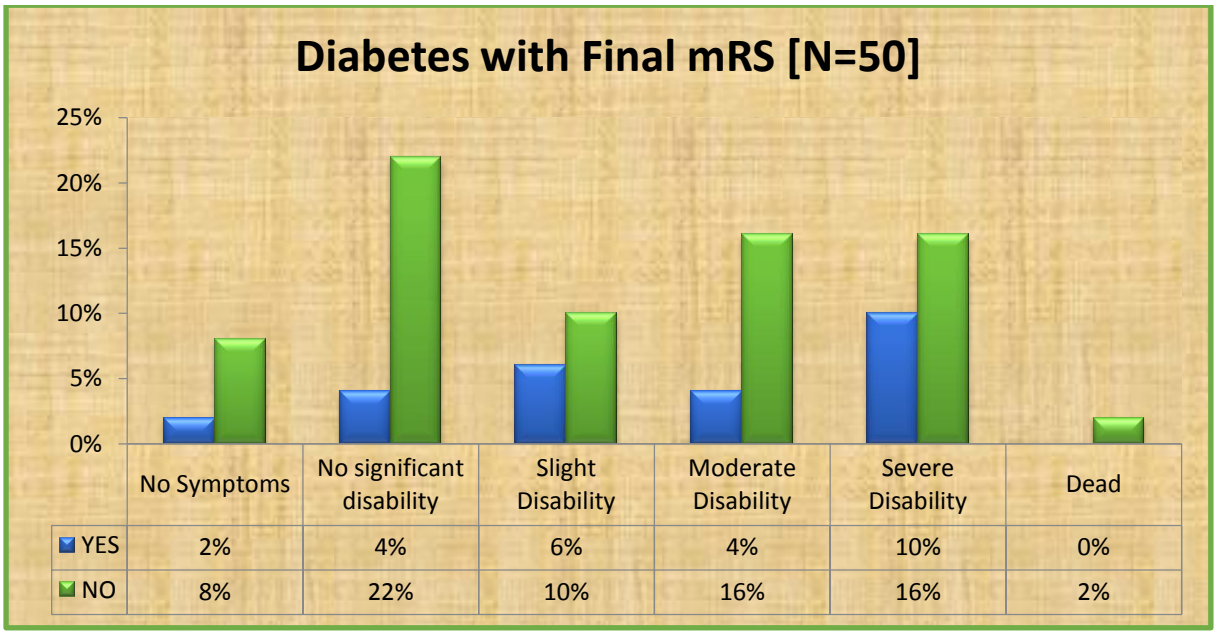
TABLE 12:

Diabetes with Final mRS score

Diabetic	FINAL mRS SCORE						Total
	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	
YES	1	2	3	2	5	0	13
NO	4	11	5	8	8	1	37
Total	5	13	8	10	13	1	50

Among the study population, 13 patients had a history of diabetes mellitus and 37 patients had no diabetes. Among the diabetics population, 5 patients had severe disability. 2 patients and 3 patients had moderate and slight disability respectively. 3 patients had complete recovery clinically. Out of which 4 had complete recovery from both signs and symptoms. Among the non-diabetic population, 1 patient had death has final outcome. 8 patients had severe disability. 8patients and 5 patients had moderate and slight disability respectively. 15 patients were observed o have complete recovery clinically, among which 4 patients were completely free of even symptoms.

FIGURE 16:



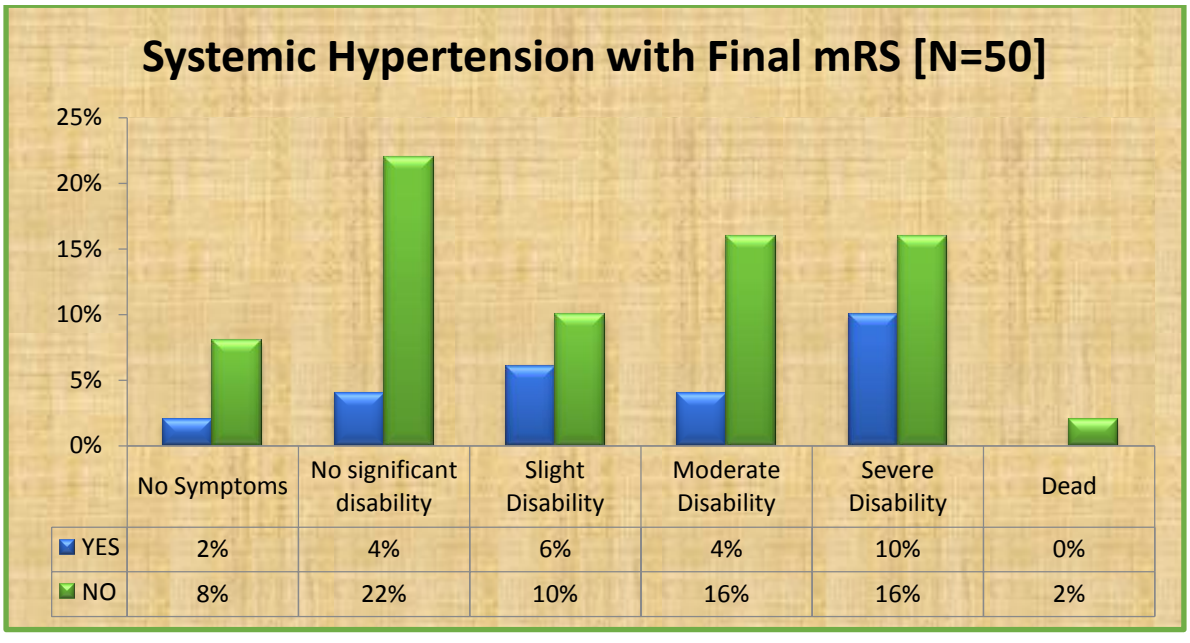
SYSTEMIC HYPERTENSION:

TABLE 13:

HYPERTENSION with Final mRS score							
	FINAL mRS SCORE						
SHT	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
YES	1	2	3	2	5	0	13
NO	4	11	5	8	8	1	37
Total	5	13	8	10	13	1	50

Among the 50 patients, 13 patients were found to have hypertension and 37 patients were non hypertensive. Among the hypertensive group, 5 patients had severe disability. 2 patients and 3 patients had moderate and slight disability. 3 patients had complete recovery clinically and among them, 1 patient was completely symptomatically free. Among the non hypertensive patients, 1 patient has death as final consequence.8 patients had severe disability. 8 patients and 5 patients had moderate and slight disability. 15 patients had complete recovery clinically, among which 4 were completely symptomatically free.

FIGURE 17:



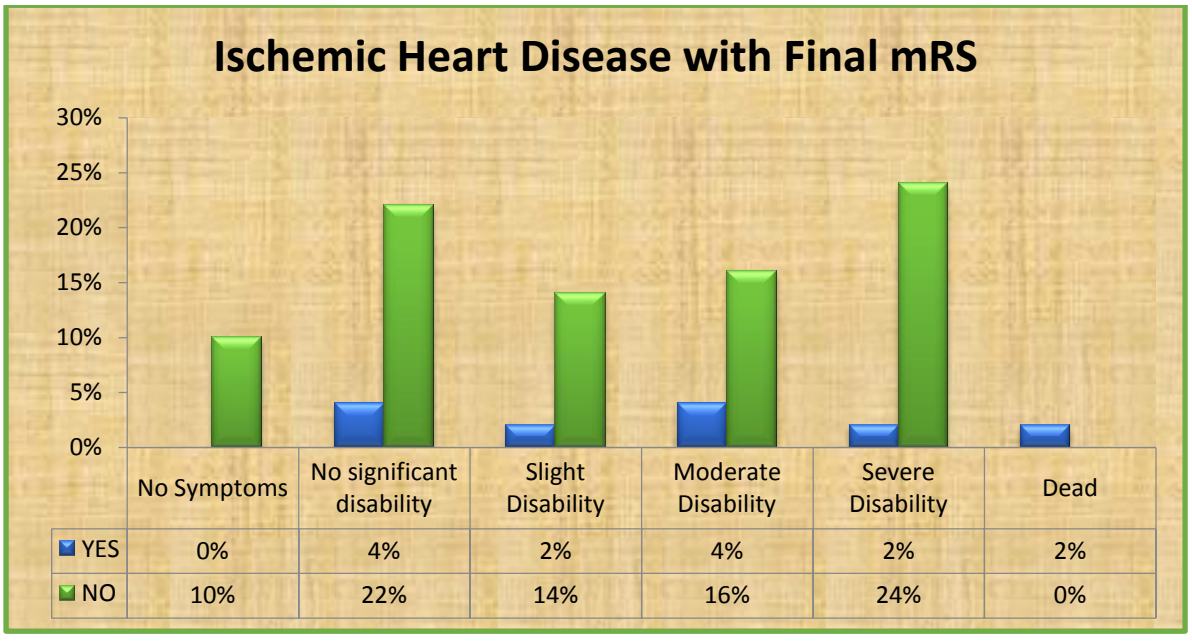
ISCHEMIC HEART DISEASE(IHD):

TABLE 14:

IHD with Final mRS score							
	FINAL mRS SCORE						
IHD	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
YES	0	2	1	2	1	1	7
NO	5	11	7	8	12	0	43
Total	5	13	8	10	13	1	50

Among the study populations, it has been observed that about patients had ischemic heart disease (IHD). 43 patients did not have any IHD. Among the HIS group of population, 1 patient had death. 1 patient had severe disability. 2 patients and 1 patient had moderate and slight disability respectively. 2 patients had complete recovery clinically. Among the non IHD group, 12 patients had severe disability. 8 patients and 7 patients had moderate and slight disability respectively. 16 patients had complete recovery from stroke clinically , among which 5 patients were completely symptomatically free.

FIGURE 18:



RECURRENT STROKE:

Among the study population, 5 patients had history of stroke presented with recurrent stroke. Among the recurrent stroke population, None had death as final consequence. 1(20%) patient had severe disability. 4 patients moderate and slight disability. 4(80%) patients had complete recovery from stroke clinically, among which 2(40%) patients were symptomatically free.

NO RISK FACTORS:

Among the study population, 3 patients had no risk factors or known comorbidities, presented with AIS. Among them, none had death as final consequence. 2 patients had severe disability. 1 patient had moderate disability. It has been observed that these patients had high NIHSS scores at presentation. They had persistent disability with no clinical improvement observed even after 3 months.

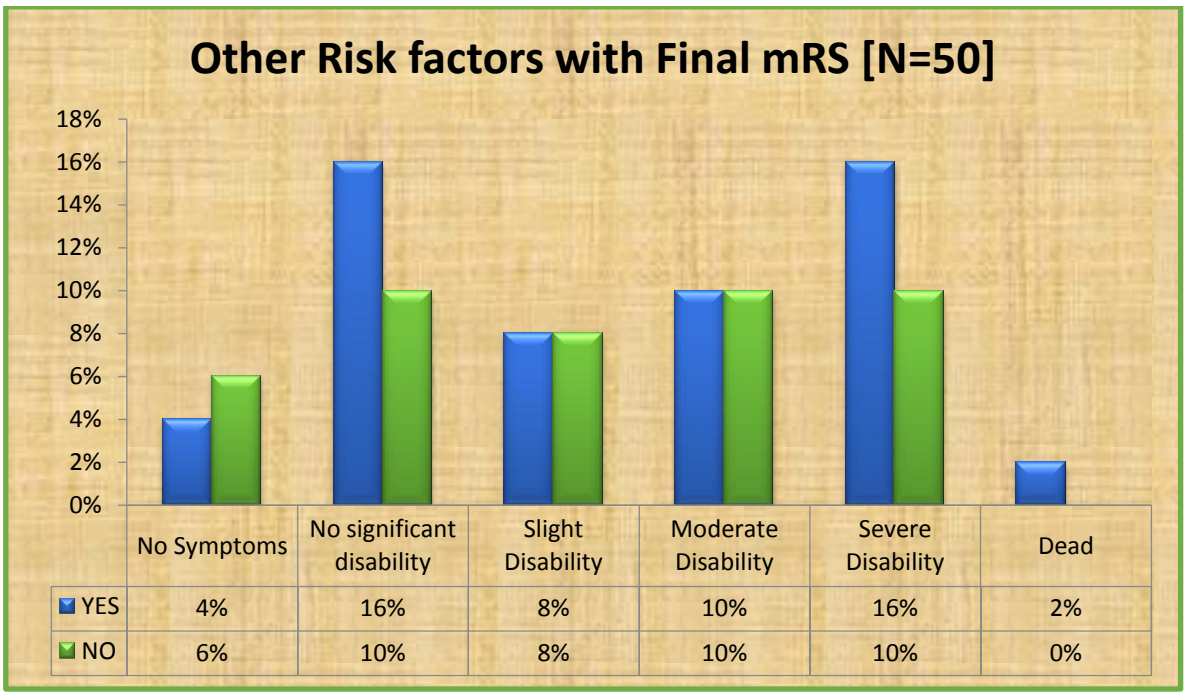
OTHERS:

TABLE 15:

Other Risk factors with Final mRS score							
	FINAL mRS SCORE						
Other Risk factors	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
YES	2	8	4	5	8	1	28
NO	3	5	4	5	5	0	22
Total	5	13	8	10	13	1	50

Among the study population, 28 patients had association of other risk factors related to occurence with AIS. These risk factors included were seizure disorder, thyroid disorder, trauma, renal failure, history of cerebral venous thrombosis. Among these population, 1 had death as final consequence. 8 patients had severe disability. 5 patients and 4 patients had moderate and slight disability. 10 patients had complete recovery from stroke clinically, among which 2 patients were symptomatically free. Among them with no other risk factors, 5 patients had severe disability. 5 patients and 4 patients had moderate and slight disability. 8 patients had complete recovery from stroke clinically, among which 3 patients were symptomatically free.

FIGURE 19:



	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead
YES	4%	16%	8%	10%	16%	2%
NO	6%	10%	8%	10%	10%	0%

TABLE 16:

CLINICAL VARIABLES WITH NIHSS SCORE							
CLINICAL VARIABLES			NIHSS				Total
			Minor Stroke	Moderate Stroke	Moderate to Severe Stroke	Severe stroke	
AGE	< 30	Count	1	2	0	0	3
		% of Total	2.00%	4.00%	0.00%	0.00%	6.00%
	31 - 35	Count	1	2	2	1	6
		% of Total	2.00%	4.00%	4.00%	2.00%	12.00%
	36 - 40	Count	6	7	3	0	16
		% of Total	12.00%	14.00%	6.00%	0.00%	32.00%
	41 - 45	Count	9	10	5	1	25
		% of Total	18.00%	20.00%	10.00%	2.00%	50.00%
SEX	Male	Count	12	19	4	1	36
		% of Total	24.00%	38.00%	8.00%	2.00%	72.00%
	Female	Count	5	2	6	1	14
		% of Total	10.00%	4.00%	12.00%	2.00%	28.00%
DLP	Yes	Count	8	11	3	2	24
		% of Total	16.00%	22.00%	6.00%	4.00%	48.00%
	No	Count	9	10	7	0	26
		% of Total	18.00%	20.00%	14.00%	0.00%	52.00%
SMOKER	Yes	Count	12	14	2	1	29
		% of Total	24.00%	28.00%	4.00%	2.00%	58.00%
	No	Count	5	7	8	1	21
		% of Total	10.00%	14.00%	16.00%	2.00%	42.00%
ALCOHOL	Yes	Count	9	14	2	1	26
		% of Total	18.00%	28.00%	4.00%	2.00%	52.00%
	No	Count	8	7	8	1	24
		% of Total	16.00%	14.00%	16.00%	2.00%	48.00%
DIABETIC	Yes	Count	5	4	4	0	13
		% of Total	10.00%	8.00%	8.00%	0.00%	26.00%
	No	Count	12	17	6	2	37
		% of Total	24.00%	34.00%	12.00%	4.00%	74.00%
SHT	Yes	Count	8	6	3	1	18
		% of Total	16.00%	12.00%	6.00%	2.00%	36.00%
	No	Count	9	15	7	1	32
		% of Total	18.00%	30.00%	14.00%	2.00%	64.00%
IHD	Yes	Count	3	2	1	1	7
		% of Total	6.00%	4.00%	2.00%	2.00%	14.00%
	No	Count	14	19	9	1	43
		% of Total	28.00%	38.00%	18.00%	2.00%	86.00%
OTHERS	Yes	Count	7	13	6	2	28
		% of Total	14.00%	26.00%	12.00%	4.00%	56.00%
	No	Count	10	8	4	0	22
		% of Total	20.00%	16.00%	8.00%	0.00%	44.00%

CLINICAL PRESENTATION

There were varied clinical presentations among the patients in this study. Out of 50 patients, 34 of them presented with motor weakness of limbs over the involved side. 9 of them presented with giddiness.3 patients had presented with blurring of vision. Whereas, about 4 patients had presented with both weakness and giddiness to the ED. One patient had presented with both weakness and blurring of vision.

Among the study patients, clinically other associated symptoms were accompanied apart from these main presenting symptoms of limb weakness, giddiness and blurring of vision. These included drowsiness, vomiting, speech abnormalities, numbness, headache, ataxia, diplopia and loss of consciousness. Among the associated complaints, 26 patients had speech abnormalities. About 10 patients were found to be drowsy at initial presentation and 8 patients had ataxia at presentation to ED. 6 patients of total had numbness, 3 patients with complaint of headache and2had complaint of vomiting during presentation to ED. Out of total study population, only one had history of loss of consciousness.

Among the study population, 34 patients presented with weakness of limbs. Out of them, 1 had death as final consequence. 11 patients had severe disability. 8 patients and 4 patients had moderate and slight disability. 10 patients had complete recovery from stroke clinically, among which 2 patients were symptomatically free. About 9 patients presented with giddiness as main presenting symptom. Among them 2 patients had severe disability.

TABLE 17:

ASSOCIATED SYMPTOMS	NUMBER (PERCENTAGE)
Speech abnormalities	26 (52%)
Drowsiness	10 (20%)
Ataxia	8 (16%)
Numbness	6 (12%)
Headache	3 (6%)
Vomiting	2 (4%)
Diplopia	1 (2%)
Loss of consciousness	1 (2%)

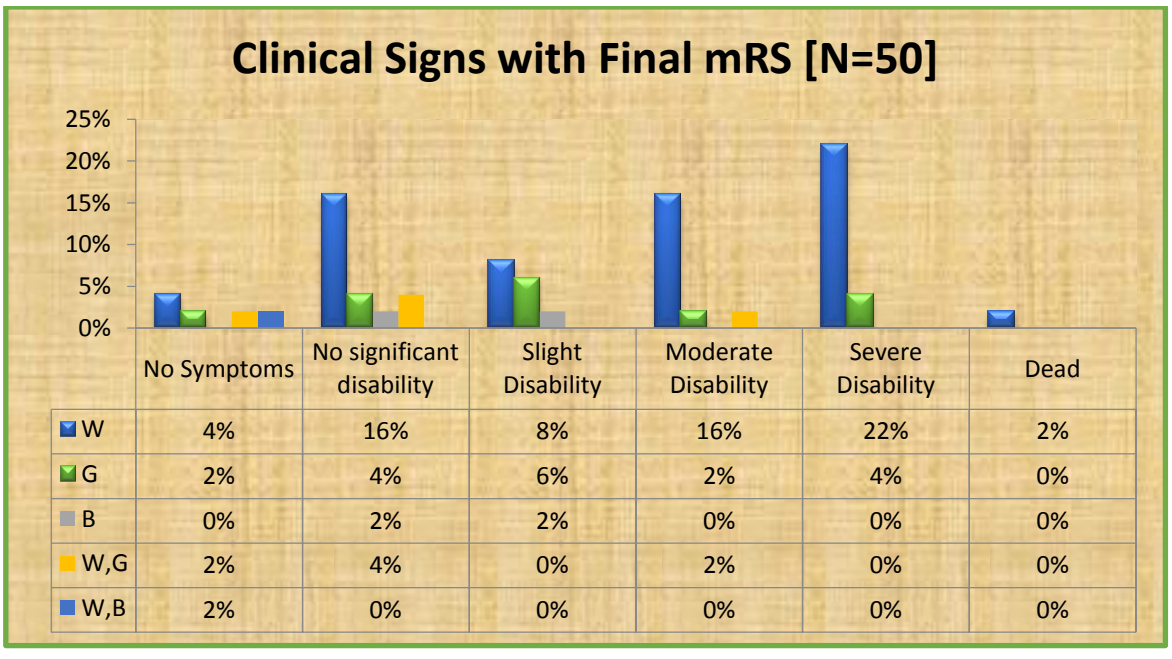
1 patient and 3 patients had moderate and slight disability. 3 patients had complete recovery from stroke clinically, among which 2 patients were symptomatically free. In the study group, 2 patients presented with blurring of vision as main presenting symptom. Out of them 1 had slight disability and 1 had complete recovery clinically and symptomatically.

TABLE 18:

Clinical Signs with Final mRS score							
	FINAL mRS SCORE						
Clinical Signs	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
Weakness(W)	2	8	4	8	11	1	34
Giddiness(G)	1	2	3	1	2	0	9
Blurring of vision(B)	0	1	1	0	0	0	2
W,G	1	2	0	1	0	0	4
W,B	1	0	0	0	0	0	1
Total	5	13	8	10	13	1	50

In the group, 4 patients had presented with both weakness of limbs and giddiness as initial manifestation. Among them, one had moderate disability.3 patients had complete recovery from stroke clinically, among which one patient was symptomatically free. And about one patient had presented with weakness and blurring of vision as initial manifestation. It was observed that this patient had complete recovery from stroke both symptomatically and clinically.

FIGURE 20:



Speech:

About 26 patients of total study population had been observed to have speech abnormalities. Among them, 1 had death as final consequence. 11 patients had severe disability. 6 patients and 3 patients had moderate and slight disability. 5 patients had complete recovery from stroke clinically, among which one patient was symptomatically free.

TABLE 19:

Speech with Final mRS score

	FINAL mRS SCORE						
Speech	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
YES	1	4	3	6	11	1	26
NO	4	9	5	4	2	0	24
Total	5	13	8	10	13	1	50

Among the population with no speech abnormalities, 2 patients had severe disability. 4 patients and 5 patients had moderate and slight disability. 13 patients had complete recovery from stroke clinically, among which 4 patients were symptomatically free.

FIGURE 21:

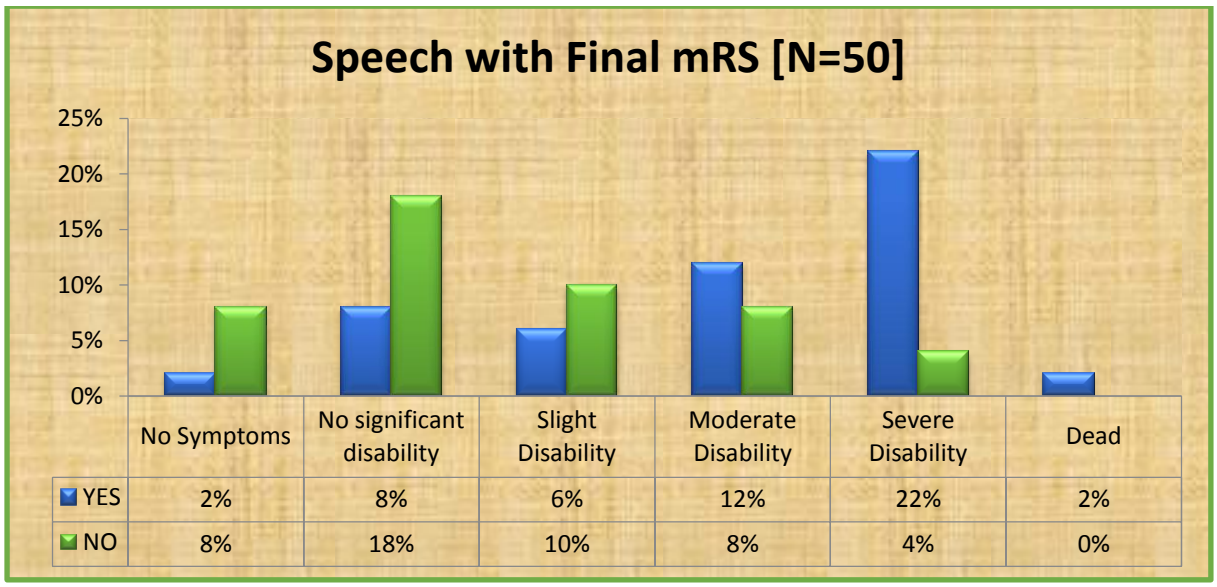


TABLE 20:

CLINICAL VARIABLES WITH NIHSS SCORE								
CLINICAL VARIABLES			NIHSS					
			Minor Stroke	Moderate Stroke	Moderate to Severe Stroke	Severe stroke	Total	
CLINICAL SIGNS		% of Total	12.00%	34.00%	18.00%	4.00%	68.00%	
	G	Count	5	3	1	0	9	
		% of Total	10.00%	6.00%	2.00%	0.00%	18.00%	
	B	Count	2	0	0	0	2	
		% of Total	4.00%	0.00%	0.00%	0.00%	4.00%	
	WG	Count	3	1	0	0	4	
		% of Total	6.00%	2.00%	0.00%	0.00%	8.00%	
	WB	Count	1	0	0	0	1	
		% of Total	2.00%	0.00%	0.00%	0.00%	2.00%	Sig
LIMBS	1	Count	5	1	1	0	7	
		% of Total	11.60%	2.30%	2.30%	0.00%	16.30%	
	2	Count	5	19	9	2	35	0.04
		% of Total	11.60%	44.20%	20.90%	4.70%	81.40%	
	4	Count	1	0	0	0	1	
		% of Total	2.30%	0.00%	0.00%	0.00%	2.30%	
SPEECH	Yes	Count	3	12	9	2	26	
		% of Total	6.00%	24.00%	18.00%	4.00%	52.00%	0.001
	No	Count	14	9	1	0	24	
		% of Total	28.00%	18.00%	2.00%	0.00%	48.00%	
SENSORY	Yes	Count	0	2	4	0	6	
		% of Total	0.00%	4.00%	8.00%	0.00%	12.00%	0.017
	No	Count	17	19	6	2	44	
		% of Total	34.00%	38.00%	12.00%	4.00%	88.00%	
CEREBELLAR	Yes	Count	1	2	1	0	4	
		% of Total	2.00%	4.00%	2.00%	0.00%	8.00%	0.941
	No	Count	16	19	9	2	46	
		% of Total	32.00%	38.00%	18.00%	4.00%	92.00%	

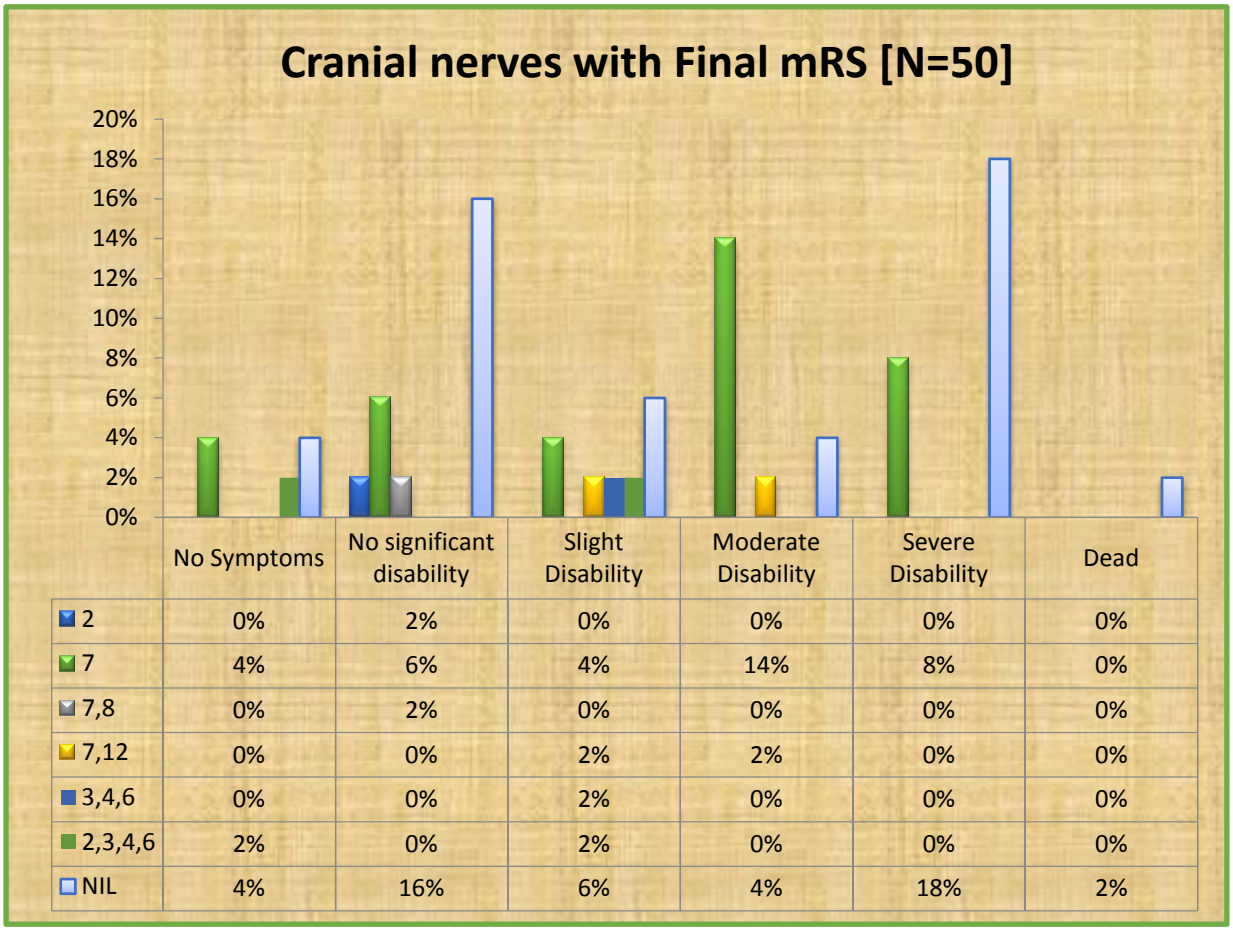
In this study, it has been observed that cranial nerve involvement was also most frequently involved among the patients with AIS. Out of 50 patients of study population, 25 patients were found to have involvement of cranial nerves. Out of which, 7th cranial nerve was most commonly affected. 7th cranial nerve involvement was seen in about 21 patients out of total 25 patients with cranial nerve involvement. Next frequently involved was seen were 3rd, 4th and 6th cranial nerves. It is observed in 3 patients of total of 25 patients associated with cranial nerve involvement. Less commonly, in one patient each 8th and 12th cranial nerves were involved respectively.

TABLE 21:

CRANIAL NERVES with Final mRS score

	FINAL mRS SCORE						
Cranial Nerves	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
2	0	1	0	0	0	0	1
7	2	3	2	7	4	0	18
7,8	0	1	0	0	0	0	1
7,12	0	0	1	1	0	0	2
3,4,6	0	0	1	0	0	0	1
2,3,4,6	1	0	1	0	0	0	2
NIL	2	8	3	2	9	1	25
Total	5	13	8	10	13	1	50

FIGURE 22:



	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead
2	0%	2%	0%	0%	0%	0%
7	4%	6%	4%	14%	8%	0%
7,8	0%	2%	0%	0%	0%	0%
7,12	0%	0%	2%	2%	0%	0%
3,4,6	0%	0%	2%	0%	0%	0%
2,3,4,6	2%	0%	2%	0%	0%	0%
NIL	4%	16%	6%	4%	18%	2%

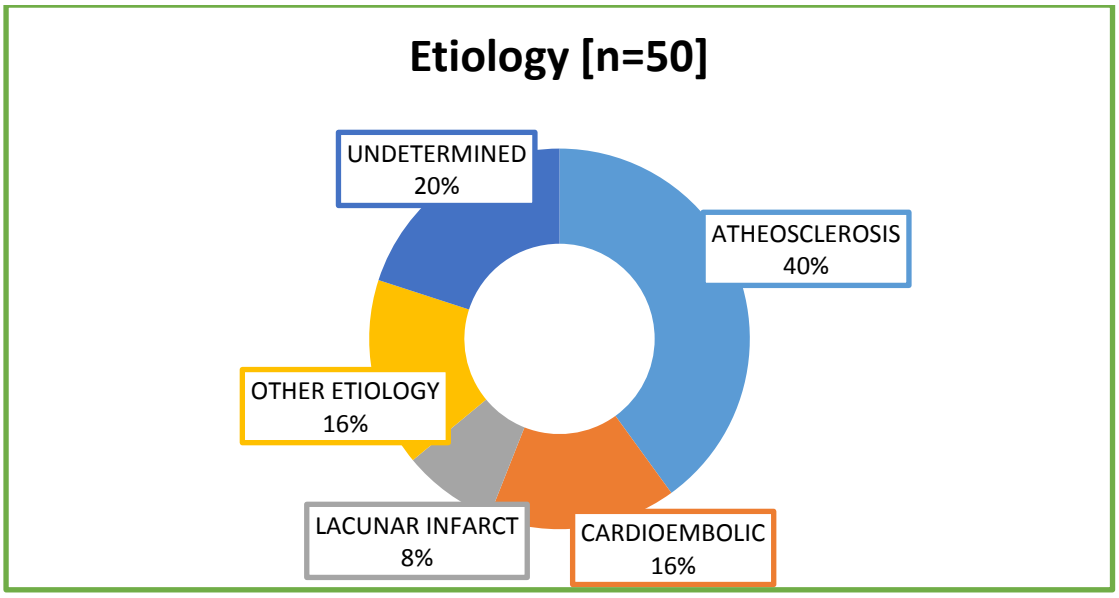
ETIOLOGY:

Stroke was classified into subtypes, according to Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria in this study. According to this criteria, 20 patients of them have had atherosclerosis as main etiological association with occurrence of stroke.About 8 patients were sub grouped to have cardio-embolic stroke. Among the 50 patients, 4 were grouped to have lacunar infarct and 9 patients were found to have stroke due to other etiology. Out of 50 patients, 9 patients were found to have stroke of undetermined etiology, where the cause of stroke in these individuals was not identified so far.

TABLE 22:

ETIOLOGY	N
ATHEROSCLEROSIS	20
CARDIOEMBOLIC	8
LACUNAR INFARCT	4
OTHER ETIOLOGY	7
UNKNOWN ETIOLOGY	11
Total	50

FIGURE 23:



Among the other etiology, involved in this study are hyperhomocystinemia (2 out of 8), antiphospholipid antibody syndrome(2 out of 8) and autoimmune causes (4 out of 8). In total, about 13 patients had hyperhomocystinemia, of which 11 had significant association with atherosclerosis causing arterial ischemic stroke in the study population.

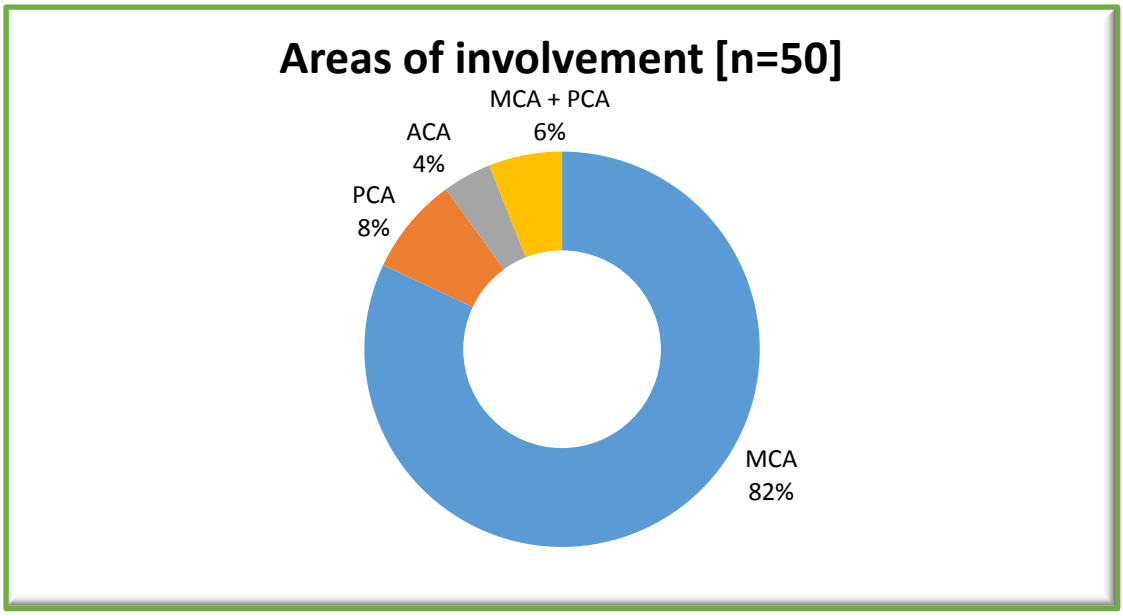
Area involved:

TABLE 23:

Areas of involvement	N
MCA	41
PCA	4
ACA	2
MCA + PCA	3

Among 50 patients in the study, 41 patients were found to have stroke involving MCA territory. 4 patients were found to have AIS involving the PCA territory. 2 patients found to have involvement of ACA territory. Out of all, 3 patients had involvement of both MCA and PCA territories

FIGURE 24:



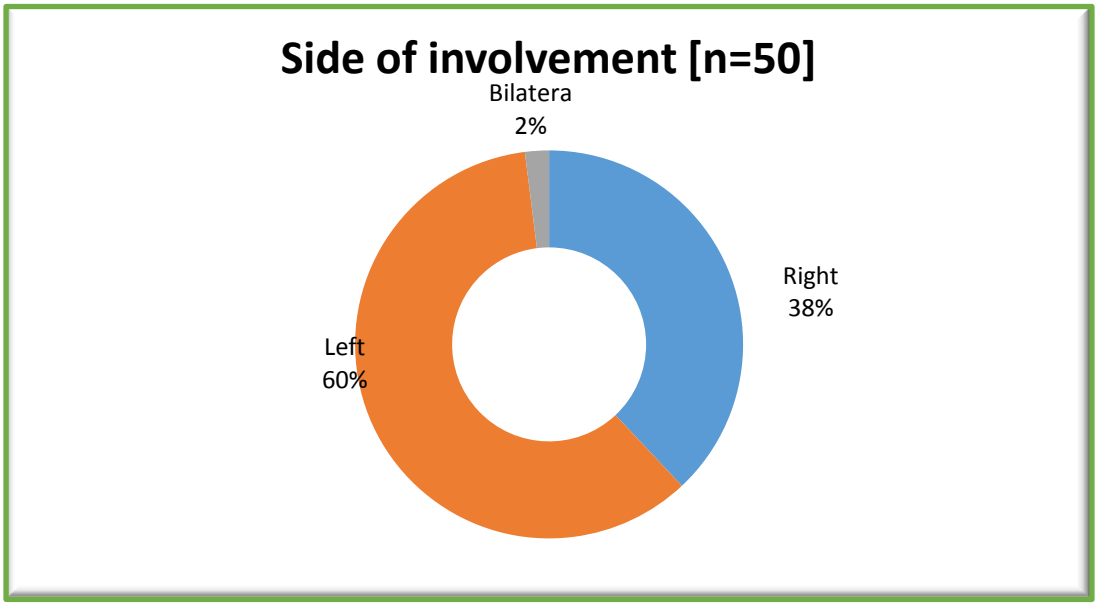
Side of involvement:

TABLE 24:

Sides of involvement	n
Right	19
Left	30
Bilateral	1

Out of 50 patients with AIS, 30 patients were found to have involvement of left sided territories. Among the 50, 19 patients found to have right sided involvement. Only one patient had involvement of both sides. Among them, apart from predominant involvement of left side, also more severity is also associated with left sided involvement at presentation based on NIHSS scoring scales at baseline. Nearly, 7 out of 30 (23%) were categorised into moderately severe to severe stroke at presentation. Right sided were categorised under minor - moderate stroke at initial presentation.

FIGURE 25:



INITIAL mRS WITH FINAL mRS:

Among the study population, about 25 patients were classified to have severe disability at initial presentation in ED. Among them, one patient had death as final consequence. 13 patients persisted to have severe disability. 11 patients had moderate disability still dependent for daily regular activities. About 2 patients had recovery with having slight disability as final outcome after 3 months of assessment.

In the study group, 10 patients had moderate disability at initial presentation to ED. Among this group of population, only one patient had persistent to have moderate disability. 3 patients had slight disability. About 6 patients of this group had total recovery clinically.

TABLE 25:

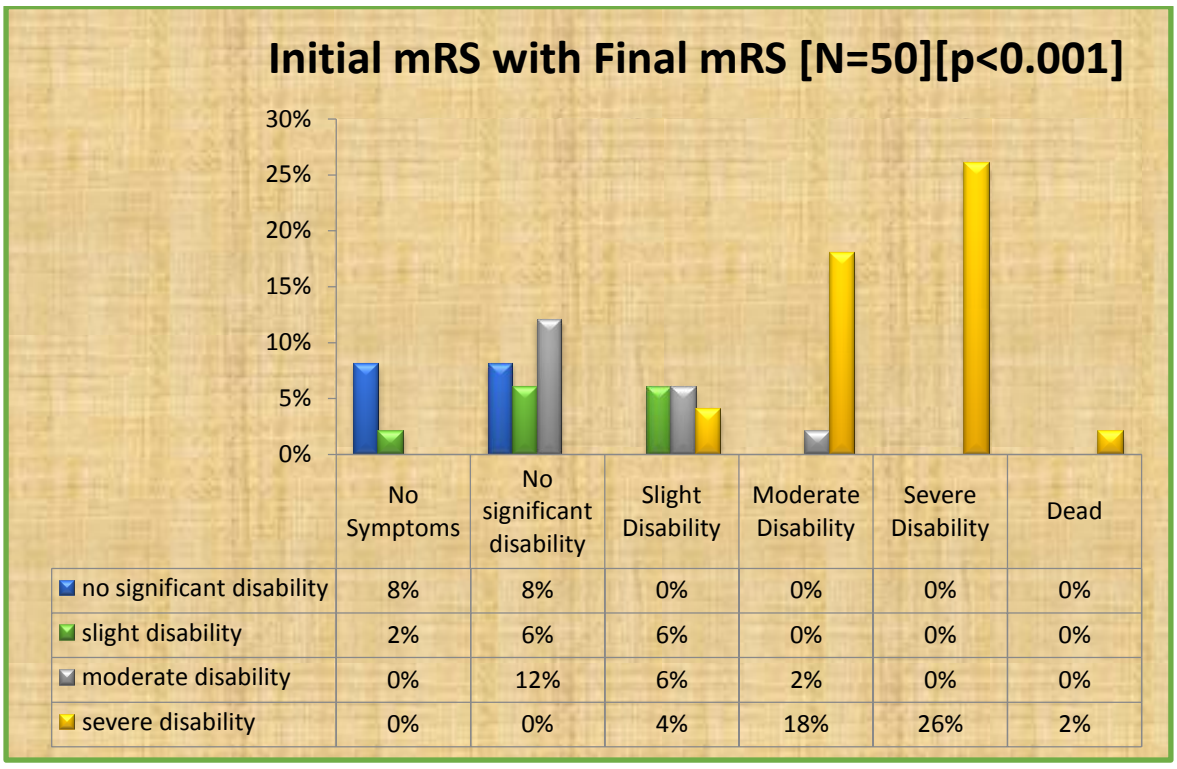
Initial MRS with Final MRS score

	FINAL MRS SCORE						
MRS	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
No significant disability	4	4	0	0	0	0	8
Slight disability	1	3	3	0	0	0	7
Moderate disability	0	6	3	1	0	0	10
Severe disability	0	0	2	9	13	1	25
Total	4	13	8	10	13	1	50

Among the study group, about 7 patients were classified to have slight disability at initial presentation in ED. Among them, 3 patients persisted to have slight disability showing no improvement. 4 patients had recovery complete recovery clinically, of which one patient showed complete symptomatic improvement.

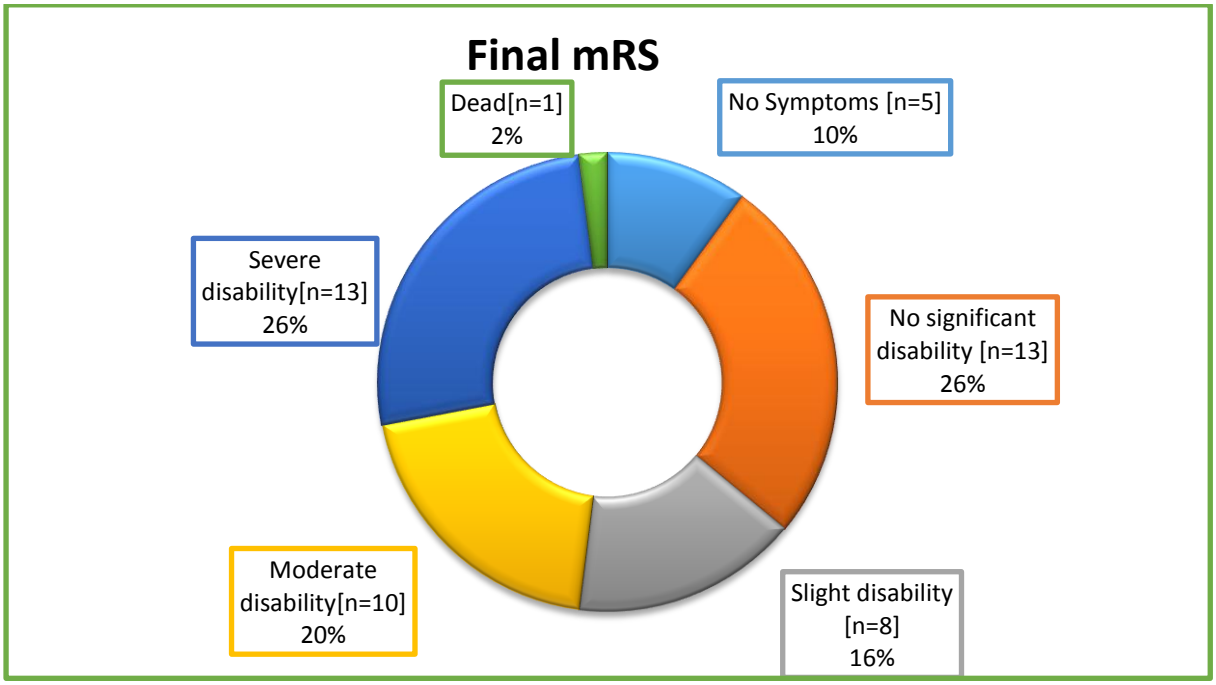
In this study group, 8 patients had no significant disability at initial presentation to ED. Among these group of population, 4 patientspersisted to have symptomatic disability. 4 patients were completely relieved of symptoms and clinically showed no disability.

FIGURE 26:



	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead
no significant disability	8%	8%	0%	0%	0%	0%
slight disability	2%	6%	6%	0%	0%	0%
moderate disability	0%	12%	6%	2%	0%	0%
severe disability	0%	0%	4%	18%	26%	2%

FINAL OUTCOME (FINAL mRS) (FIGURE 27):



FINAL OUTCOME (FINAL mRS) WITH INITIAL NIHSSSCORING:

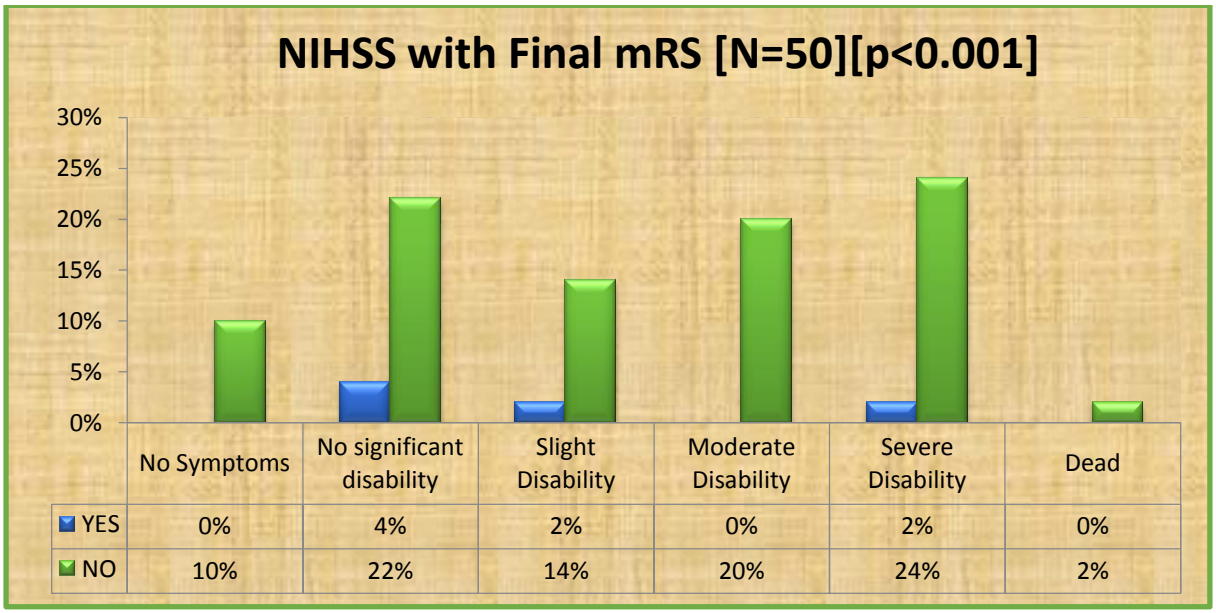
About of total of 50 patients involved in the study, patients were given NIHSS scoring at initial presentation in ED. Outof 50 patients, 2 patients presented with severe stroke with NIHSS scoring between 21-42, of which one patient had death as final outcome and other patient had slight disability.About 10 patients were classified to have moderate to severe stroke with NIHSS scoring of 16-20. Among this group, 6 patients had severe disability. 3 patients had moderate disability and one patient had improvement with slight disability as final outcome.

TABLE 26:

NIHSS with Final mRS score							
	FINAL mRS SCORE						
NIHS	No Symptoms	No significant disability	Slight Disability	Moderate Disability	Severe Disability	Dead	Total
Minor Stroke	5	7	5	0	0	0	17
Moderate Stroke	0	6	1	7	7	0	21
Moderate to Severe Stroke	0	0	1	3	6	0	10
Severe stroke	0	0	1	0	0	1	2
Total	5	13	8	10	13	1	50

About 21 patients were classified under moderate stroke with NIHSS scoring of 5-15. Among this study population, 7 patients had persistent severe disability. 7 patients had moderate disability and one patients had slight disability. 6 patients found to have complete recovery clinically. About 17 patients presented to ED initially were classified to have minor stroke according to NIHSS scoring of 0-4. Out of which, 5 had slight disability as final outcome after 3 months. 12 patients had complete recovery clinically, of which 5 patients had completely symptomatic free.

FIGURE 28:



DISCUSSION

Stroke among young adults has been increasing in incidence in the recent times. Identification of risk factors and etiology play a crucial role in reducing the morbidity and financial burden in the society.

In this study, 50 consecutive cases of stroke among young individuals fulfilling inclusion and exclusion criteria were taken in the study.

- In concordance with the other studies in India, predominance of stroke was seen among males in study population(36 out of 50).The mean age observed was 39 years, with highest incidence of stroke was seen in 4th decade accounting about 50% falling between the age group 40-45years.
- Smoking, alcoholism and dyslipidemia have been found to be significantly associated with stroke. Whereas, other studies from India showed smoking, diabetes and hypertension to be prevalant risk factors. Diabetes and ischemic heart disease was found to have a very low association with the occurence of stroke among young individuals in the study.
- Hyper-homocystinemia has significant association with the causation of stroke in the young individuals. Of which, 18.4% was observed with atherosclerosis contributing to the evidence of its pro-thrombotic role in occurrence of stroke in the young adults.
- Recurrence of stroke though was seen in 10%, but no mortality and less morbidity has been observed among these patients. Patients with no known

associated risk factors were found to have initial severe presentation with persistent clinical morbidity.

- Most common clinical finding was hemiplegia with seventh cranial nerve palsy. Majority have left sided involvement associated with significant speech abnormalities, observed in this study. They have significant association with prolonged morbidity compared to that among right sided involvement.
- In concordance with other studies in India, Atherosclerosis remains the major etiological association of ischemic stroke in this study. Whereas, still in about 20% of total population, etiology of arterial ischemic stroke was undetermined.
- Vitamin D deficiency also has contributory role among the dividuals affected with stroke. With respect to a meta-analysis in August 2012, risk of stroke was observed with Vitamin D deficiency among the study population due to its effect on the vasculature. It also has long term effect on morbidity among stroke patients.
- NIHSS scoring scale is one among the best scoring scales for predicting the outcome and prognosis of the young individuals presented with stroke. NIHSS scoring at initial presentation, most of them were graded to have moderate and minor stroke. Significant disability seen among the individuals with higher NIHSS scores at baseline there by increase in morbidity.
- Initial mRS scoring also has significant impact on the final outcome among the study population. Initially with severe disability were found to have persistent disability even after three months thereby increasing the morbidity and affecting the financial and economic aspects of family.

CONCLUSION

- Stroke among young individuals is a major health issue and remains a diagnostic challenge comparatively to that among elderly.**(40)** It is anticipated that increase in prevalence of stroke among young individuals by 2050. **(34, 35)**
- In this study , males have higher incidence of developing stroke compared to females (Male : Female = 2.6 : 1)
- Most of the study population, are among age group between 41-45years. The least age observed to have developed stroke is 21 years.
- It has been observed that smoking, alcohol,dyslipidemia are the modifiable risk factors in the decreasing order of frequency found to have significant association occurring in higher incidence among the study population
- Whereas, incidence of heart diseases, diabetes and family history observed to be low in this study.With no underlying risk factors, there was found to have higher morbidity.
- Clinically, weakness was the predominant symptom observed. Speech involvement has a higher incidence and also has significant impact on final outcome among the study population. Involvement of seventh cranial nerve is frequently observed among the study group.
- Atherosclerosis was the main etiological association with young stroke in this study.

- Despite the lack of absolute accuracy of classification models, scoring systems that have good predictive accuracy can play an important role in assessing the severity and outcome of stroke. they also help in prognostication of patients with acute stroke.
- Proper history taking plays a major role among the young population. Identification and modification of risk factors have a consequential effect on the individual and the society.
- Vitamin D deficiency has both causative and long term effect among the stroke patients. More studies are needed for its in role in occurence of stroke and also its impact on the morbidity.
- Extensive etiological evaluation for the stroke in young individuals is needed and managed accordingly which has a significant impact on the outcome of the individuals.

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PROFORMA

- Name
- Age
- Sex
- Address
- Occupation
- Chief complaints
- H/o cocaine abuse or any other substance abuse or use of oral contraceptives
- H/o smoking, alcohol, diabetes, hypertension, seizure disorder, bleeding disorders, migraine, thrombosis, rheumatic heart disease, ischaemic heart disease, severe LV dysfunction, arrhythmias (mainly atrial fibrillation)
- H/o head trauma
- Family history of thrombosis, hyperlipidaemia, hypertension, diabetes

CLINICAL EXAMINATION

- General examination
- CNS examination:
  - Speech – dysarthria or aphasia (motor / sensory/ global)
  - Cranial nerves
  - Weakness of limb – 1 UL or 1 UL and 1 LL or 4 limbs
  - Power – UL and LL
  - Sensory
  - Cerebellar
  - Carotid and subclavian bruits, murmurs
  - Peripheral pulses
  - NIHSS on admission
  - mRS on admission and after 3 months
- Routine investigations:
  - Complete blood count, Diabetic profile
  - Serum electrolytes, urine routine and microscopy
  - ECG, ECHO, serum homocysteine levels
  - CT- brain plain, MRI brain with angiography
- Other investigations:
  - ANA IF and Antiphospholipid antibodies
- If needed:
  - Complete coagulation work up
  - Genetic testing

ABBREVIATIONS

AIS	–	Arterial ischemic stroke
WHO	-	World Health Organization
TOAST	-	Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.
ANA	–	Anti nuclear antibody profile
APLA	–	Anti-phospholipid antibody
CT	–	Computed tomography
MRI	–	Magnetic resonance imaging
NIHSS	-	National Institute of Health stroke scale
mRS	–	modified rankin scoring
TIA	-	Transient ischemic attacks
ICMR	-	Indian Council Medical Research
DALY	-	disability life adjusted years
LDL-C	-	low-density lipoprotein cholesterol
TGL	-	Triglycerides
HDL-C	-	High-density lipoprotein cholesterol (HDL-C)
BMI	–	Body mass index

SBP	–	Systolic blood pressure
DBP	–	Diastolic blood pressure
FBS	-	fasting blood glucose
HbA1c	-	glycosylated haemoglobin
DM	–	Diabetes mellitus
MA	–	Migraine headache with aura
ECMO	–	Extracorporeal membrane oxygenation
RHD	-	Rheumatic heart disease
DCM	-	Dilated cardiomyopathy
AMI	–	Acute myocardial infarction
IE	–	Infective endocarditis
AF	–	Atrial Fibrillation
CAD	–	Coronary artery disease
LVH	–	Left ventricular hypertrophy
LAE	–	Left atrial enlargement
CBS	–	Cystathione b-synthase
PV	–	Polycthemiavera
ET	-	Essential thrombocythemia

PAN	–	Polyarteritisnodosa
WG	–	Wegener’s granulomatosis
CNS	-	Central nervous system
CADASIL	–	Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
CARASIL	–	Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy
MELAs	–	Mitochondrial myopathy, encephalopathy, lacto-acidosis and stroke
EDS	–	Ehlers Danlos syndromes
OI	–	Osteogenenis imperfect
ADPKD	-	Autosomal dominant polycystic kidney disease
LDS	-	Loeyz Dietz syndrome
AD	–	Autosomal dominant
COW	–	Circle of willis
ACA	–	Anterior cerebral artery
MCA	–	Middle cerebral artery
PCA	–	Posterior cerebral artery
UMN	–	Upper motor neuron type

ED	–	emergency department
HIV	–	human immunodeficiency virus
ECG	–	Electrocardiogram
ECHO	–	Echocardiography
AHA/ASA	–	American heart association / American stroke association
r-tPA	–	Recombinant tissue plasminogen activator
NINDS	–	National institute of Neurological Disorders and Stroke
aPTT	–	Activated partial thromboplastin time
INR	–	International normalised ratio
PT	–	Prothrombin time
UFH	–	Unfractionated heparin
LMWH	–	Low molecular weight heparin

CONSENT FORM

PSG Institute of Medical Science and Research, Coimbatore
Institutional Human Ethics Committee
INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

(strike off items that are not applicable)

I / We (write name of the investigator(s) here), Dr. KARRI MADHAVI, am carrying out a study on the topic: ETIOLOGY AND CLINICAL OUTCOME OF STROKE IN YOUNG ADULTS(18-45years) ADMITTED IN A TERTIARY CARE HOSPITAL.

as part of my / our research project being carried out under the aegis of the Department of: GENERAL MEDICINE

(*Applicable to students only*): My / our research guide is: Dr. SUJITH KUMAR S M.D

The justification for this study is:
Considering the disease burden and the morbidity and mortality associated with specific etiology of stroke in young adults admitted which is essential to reduce the socioeconomic burden in the family, to treat and also for further prevention of recurrence.

The objectives of this study are:

Primary Objective: To study the etiology and clinical outcome in stroke of young adults

Secondary Objective: To know the morbidity and mortality in the stroke of young adults

Sample size: 50

Study volunteers / participants are (specify population group & age group): Patients between 18-45years admitted with stroke

Location: PSG Hospitals, Coimbatore.

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:

Initial interview (specify approximate duration):_____ minutes.

Data collected will be stored for a period of __TWO__ years. We will / will not use the data as part of another study.

Health education sessions: Number of sessions: _____. Approximate **duration** of each session:

_____ minutes.

Clinical examination (Specify details and purpose): To assess the general condition and systemic examination

Blood sample collection: Specify quantity of blood being drawn: __5__ml.

No. of times it will be collected: ONCE

Whether blood sample collection is part of routine procedure or for research (study) purpose: RESEARCH

1. Routine procedure 2. Research purpose

Specify **purpose**, discomfort likely to be felt and side effects, if any: __NIL___

Whether blood sample collected will be stored after study period: No, it will be destroyed

Whether blood sample collected will be sold: No

Whether blood sample collected will be shared with persons from another institution: No

Medication given, if any, duration, side effects, purpose, benefits: NIL

Benefits from this study: TO ASSESS THE ETIOLOGY SO THAT IT CAN BE USED FOR PRIMARY AND SECONDARY PREVENTION OF STROKE IN YOUNG ADULTS (18-45 YEARS).

Risks involved by participating in this study: NIL

How the **results** will be used: Study will be submitted to Dr. MGR Medical University as thesis in post graduate course in general medicine.

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date:

Witness:

Contact number of PI: 08754189611

Contact number of Ethics Committee Office: 0422 2570170 Extn.: 5818

ஒப்புதல் படிவம்

தேதி :

கரி மாதவி, ஆகிய நான், பி. எஸ். ஜி. மருத்துவக் கல்லூரியின், பொது மருத்துவ துறையின் கீழ், **"மூன்றாம் நிலை மருத்துவமனையில் அனுமதிக்கப்படும் இளம் வயதில் (18-45 வயதிற்குள்) ஏற்படும் பக்கவாதத்திற்கான காரணங்களும், விளைவுகளும்"** என்ற தலைப்பின் கீழ் ஆய்வு மேற்கொள்ள உள்ளேன்.

என் ஆய்வு வழிகாட்டி: மருத்துவர். சுஜித்குமார்

ஆய்வு மேற்கொள்வதற்கான அடிப்படை:
நோய்க்கான காரணத்தை அறிவதன் மூலம் மறுபடியும் அந்நோய் முற்றுவதை தடுக்க முடியும் மேலும் அதனால் ஏற்படும் செலவீணத்தையும் தடுக்கலாம்.

ஆய்வின் நோக்கம்:
இளம் வயதில் ஏற்படும் பக்கவாதத்தின் காரணத்தியும், விளைவுகளையும் மேலும் அதனால் ஏற்படும் ஆபத்தையும் கண்டறிவது.

ஆய்வில் பங்கு பெறும் நபர்களின் எண்ணிக்கை: 50

ஆய்வு மேற்கொள்ளும் இடம்: பி. எஸ். ஜி. மருத்துவமனை, கோயம்புத்தூர்.

ஆய்வின் பலன்கள்:
நோய் வருமுன் தடுக்கவும் வந்தபின் சிகிச்சை அளிக்கவும் உதவும்.

ஆய்வினால் ஏற்படும் அசௌகரியங்கள் / பக்க விளைவுகள்: பக்க விளைவுகள் எதுவும் இல்லை.

இந்த ஆய்வில் கிடைக்கும் தகவல்கள் ____ வருடங்கள் பாதுகாக்கப்படும். இவை தேவைப்பட்டால் வேறு ஆய்விற்கும் பயன்படுத்தப்படலாம். எந்த நிலையிலும் உங்களைப் பற்றிய தகவல்கள் யாருக்கும் தெரிவிக்கப்படமாட்டாது. அவை இரகசியமாக வைக்கப்படும்.

இந்த ஆய்வில் பங்கேற்க ஒப்புக்கொள்வதால் எந்த விதமான பலனும் உங்களுக்கு கிடைக்காது. எந்த நேரத்தில் வேண்டுமானாலும் ஆய்விலிருந்து விலகிக்கொள்ளும் உரிமை உங்களுக்கு உண்டு. ஆய்விலிருந்து விலகிக்கொள்வதால் உங்களுக்கு அளிக்கப்படும் சிகிச்சையில் எந்த வித மாற்றமும் இருக்காது.

இந்த ஆராய்ச்சிக்காக உங்களிடம் சில கேள்விகள் கேட்கப்படும் / சில இரத்த மாதிரிகள் அல்லது திசு மாதிரிகள் எடுக்கப்படும்.

மேலும், இந்த ஆய்வில் பங்கு கொள்வது உங்கள் சொந்த விருப்பம். இதில் எந்த விதக் கட்டாயமும் இல்லை. நீங்கள் விருப்பப் பட்டால், இந்த ஆய்வின் முடிவுகள் உங்களுக்குத் தெரியப் படுத்தப்படும்.

ஆய்வாளரின் கையொப்பம் :
தேதி :

ஆய்வுக்குட்படுபவரின் ஒப்புதல்:

நான் இந்த ஆராய்ச்சியின் நோக்கம் மற்றும் அதன் பயன்பாட்டினைப் பற்றி தெளிவாகவும், விளக்கமாகவும் தெரியப்படுத்தப் பட்டுள்ளேன். இந்த ஆராய்ச்சியில் பங்கு கொள்ளவும், இந்த ஆராய்ச்சியின் மருத்துவ ரீதியான குறிப்புகளை வரும் காலத்திலும் உபயோகப்படுத்திக் கொள்ளவும் முழு மனதுடன் சம்மதிக்கிறேன்.

ஆய்வுக்குட்படுபவரின் பெயர், முகவரி :

கையொப்பம் :
தேதி :

ஆய்வாளரின் தொலைபேசி எண்: 8754189611
மனித நெறிமுறைக் குழு அலுவலகத்தின் தொலைபேசி எண்: 0422 2570170 Extn.: 5818

வினாத்தாள்

பெயர் (Name):

வயது/பாலினம் (Age/Sex):

முகவரி (Address):

தொழில் (Occupation):

குறைகள்:

குடும்பத்தில் யாருக்கேனும் புகை பிடித்தல், மது அருந்துதல், சக்கரை வியாதி, இரத்த அழுத்தம், வலிப்பு, இரத்தக்கசிவு வியாதி, தலைவலி, இரத்த குழாய் அடைப்பு, இருதய நோய், கொழுப்பு, கருத்தடை உபயோகித்தல், தலையில் அடி உள்ளதா?

MASTER CHART 1:

SLNO	IP NO	OP NO	AGE	SEX	DLP	SMOKER	ALCOHOLIC	DIABETES	HYPERTENSION	IHD	OTHERS	CLINICAL SIGNS	CN	SPEECH
1	I14023014	O14055620	45	1	N	Y	Y	N	N	N	N	1	1	N
2	I14021240	O14050720	39	1	Y	Y	Y	N	N	N	Y	1	1	N
3	I15007075	O14050515	45	1	N	Y	Y	N	N	N	Y	1	1,2	N
4	I14016935	O14040111	40	2	N	Y	N	N	Y	N	Y	2		Y
5	I14020097	O10081131	45	1	N	Y	Y	Y	Y	Y	N	3	2	N
6	I14020828	O14049567	45	1	N	Y	Y	N	N	N	N	1,2		N
7	I14028157	O14068546	44	2	N	N	N	N	N	N	N	2		Y
8	I14029146	O14070542	37	1	N	Y	N	N	N	N	Y	1	1	Y
9	I14027926	O14067826	42	1	Y	Y	N	Y	N	N	Y	1	1	Y
10	I14024384	O14057421	38	1	Y	Y	Y	N	Y	N	Y	1		Y
11	I14027826	O14067618	45	1	N	Y	N	N	N	N	Y	1	1	Y
12	I14021842	O14052378	38	1	Y	Y	Y	Y	Y	N	N	12		N
13	I14022448	O14054085	43	1	Y	Y	Y	Y	Y	N	N	1,2	1	N
14	I14022885	O14055319	32	2	Y	N	N	N	Y	N	R	1	1	N
15	I14025003	O14061491	44	2	Y	N	N	N	N	N	Y	1		N
16	I14025959	O12047986	43	1	N	Y	Y	N	Y	N	Y	1	1	N
17	I14026399	O14064697	34	2	Y	N	N	N	N	N	N	1	1,2	Y
18	I15001731	O15003942	45	1	Y	Y	Y	N	N	N	Y	1		Y
19	I15001790	O15003988	43	2	N	N	N	N	Y	N	N	1	1	Y
20	I15001354	O15002877	41	1	N	Y	N	Y	N	N	Y	1		Y
21	I14029678	O12069010	41	1	N	Y	Y	N	N	Y	Y	1		Y
22	I14035213	O14077668	45	2	Y	N	N	Y	Y	N	Y	1		Y
23	I15003835	O15008164	39	1	N	Y	Y	N	N	N	N	1		N
24	I15004238	O15009237	39	2	Y	N	N	N	N	Y	Y	2		Y
25	I15005388	O15012108	21	1	N	N	N	N	N	N	Y	1		N

MASTER CHART 2:

SLNO	IP NO	OP NO	AGE	SEX	DLP	SMOKER	ALCOHOLIC	DIABETES	HYPERTENSION	IHD	OTHERS	CLINICAL SIGNS	CN	SPEECH
26	I15004664	O09096593	32	2	Y	N	N	N	Y	Y	Y	1		Y
27	I15005072	O15000789	40	1	N	Y	Y	N	N	N	R	1,2		N
28	I15004684	O15010392	44	1	Y	N	N	Y	Y	N	N	2	2	N
29	I15010881	O15023932	43	2	N	N	N	N	N	N	N	1		N
30	I15009338	O15020584	40	1	Y	Y	Y	Y	Y	Y	N	3	2	N
31	I15009422	O15008011	45	1	Y	Y	Y	N	N	N	N	2		N
32	I15010478	O15023091	39	1	Y	Y	Y	N	N	N	Y	1	1	Y
33	I15010659	O15023491	41	1	Y	N	Y	N	Y	N	N	1		N
34	I14013591	O14005098	36	1	Y	N	Y	N	N	N	Y,R	1		Y
35	I14017342	O14041004	40	1	Y	Y	Y	N	N	Y	Y	1	1	N
36	I14017359	O14041034	27	1	N	N	Y	N	N	N	Y	1	1	N
37	I15013007	O15028542	45	1	N	N	N	Y	Y	N	N	1		N
38	I15013724	O13022404	31	2	N	N	N	N	N	N	N	1	1	Y
39	I15012975	O15018487	43	2	N	N	N	Y	N	N	Y	1	1	Y
40	I15011843	O15025787	36	1	N	N	N	N	Y	N	N	2		Y
41	I15011247	O15024729	45	1	Y	Y	Y	Y	N	N	N	1		N
42	I15013023	O15028557	40	1	N	Y	Y	N	N	N	Y	1		Y
43	I15007755	O15015365	32	1	N	Y	Y	N	N	N	N	1	1	Y
44	I15007826	O10090386	41	1	Y	Y	N	N	Y	Y	Y	1	1	Y
45	I15008171	O12070416	20	2	N	N	N	N	N	N	Y	1,2	1	Y
46	I14029157	O14070555	44	1	Y	N	Y	Y	Y	N	R	1	1	Y
47	I15011176	O15024458	36	1	N	Y	N	N	N	N	N	1,3	2	N
48	I14015373	O14035826	39	1	Y	Y	Y	N	Y	N	R	2		Y
49	I15006300	O15013834	45	1	Y	Y	Y	Y	N	N	N	2		N
50	I15007697	O15016774	32	2	N	N	N	N	N	N	N	1	1,2	Y

MASTER CHART 3:

SLNO	IP NO	OP NO	HYPER-HC	AREA	SIDE	ETIOLOGY	NIHSS	INITIAL MRS	FINAL MRS(AT 3MONTHS)
1	I14023014	O14055620	A	1	1	5	2	4	3
2	I14021240	O14050720	A	1	1	1	2	3	2
3	I15007075	O14050515	P	1	1	1	2	1	1
4	I14016935	O14040111	A	1	2	2	1	2	2
5	I14020097	O10081131	A	3	2	2	1	1	1
6	I14020828	O14049567	A	1	2	1	1	3	1
7	I14028157	O14068546	A	1	2	2	2	5	4
8	I14029146	O14070542	P	1	1	1	2	5	3
9	I14027926	O14067826	P	1	2	1	2	1	1
10	I14024384	O14057421	A	1	2	1	2	5	5
11	I14027826	O14067618	A	1	1	5	2	3	1
12	I14021842	O14052378	A	1,3	2	1	1	2	2
13	I14022448	O14054085	A	1	2	1	2	4	3
14	I14022885	O14055319	A	2	1	3	1	1	0
15	I14025003	O14061491	A	1	1	2	1	2	1
16	I14025959	O12047986	A	1	2	2	1	2	2
17	I14026399	O14064697	A	1	2	1	2	3	3
18	I15001731	O15003942	A	1	2	5	4	5	2
19	I15001790	O15003988	A	1	2	5	3	5	3
20	I15001354	O15002877	A	1	2	5	3	5	5
21	I14029678	O12069010	P	1	2	4	2	5	4
22	I14035213	O14077668	A	2	2	5	3	5	3
23	I15003835	O15008164	A	1	1	4	1	3	1
24	I15004238	O15009237	A	1	2	4	3	5	3
25	I15005388	O15012108	P	1	1	4	2	3	1

MASTER CHART 4:

SLNO	IP NO	OP NO	HYPER-HC	AREA	SIDE	ETIOLOGY	NIHSS	INITIAL MRS	FINAL MRS(AT 3MONTHS)
26	I15004664	O09096593	A	1	2	5	4	5	6
27	I15005072	O15000789	A	1	2	5	1	1	1
28	I15004684	O15010392	A	1	1	1	1	4	2
29	I15010881	O15023932	A	1	2	1	1	1	0
30	I15009338	O15020584	A	1,3	2	3	1	3	2
31	I15009422	O15008011	A	3	1	5	1	3	1
32	I15010478	O15023091	A	1,3	1	5	2	5	4
33	I15010659	O15023491	A	1	2	1	2	3	1
34	I14013591	O14005098	A	1	2	1	3	5	5
35	I14017342	O14041004	A	1	2	2	2	4	3
36	I14017359	O14041034	A	1	2	2	2	5	3
37	I15013007	O15028542	A	1	1	3	3	5	4
38	I15013724	O13022404	A	1	2	4	3	5	5
39	I15012975	O15018487	A	1	2	1	3	5	4
40	I15011843	O15025787	A	3	1,2	3	2	5	4
41	I15011247	O15024729	A	1	1	1	2	5	4
42	I15013023	O15028557	P	1	2	1	3	5	5
43	I15007755	O15015365	P	1	1	1	2	4	3
44	I15007826	O10090386	A	1	1	1	1	2	1
45	I15008171	O12070416	A	1	2	4	1	2	0
46	I14029157	O14070555	A	1	1	1	2	5	4
47	I15011176	O15024458	A	1	2	2	1	1	0
48	I14015373	O14035826	A	1	2	1	2	2	1
49	I15006300	O15013834	P	3	1	4	1	1	0
50	I15007697	O15016774	A	1	1	5	3	3	2

MASTER KEY CHART 1 AND 2

SEX –

1 - MALE

2 - FEMALE

Y=YES

N=NO

CLINICAL SIGNS:

1 - WEAKNESS

2 - GIDDINESS

3 - BLURRING

CRANIAL NERVES (CN):

1 - SEVENTH CRANIAL NERVE

2 - OTHER CRANIAL NERVES

DLP - DYSLIPIDEMIA

CHART 3 AND 4:

HYPERHOMOCYSTINEMIA

P=PRESENT

A=ABSENT

AREA-

1 - MCA

2 - ACA

3 - PCA

SIDE

1 - RIGHT

2 - LEFT

ETIOLOGY

1 - ATHEROSCLEROSIS

2 - CARDIOEMBOLIC

3 - LACUNAR INFARCT

4 - OTHER ETIOLOGY

5 - UNKNOWN ETIOLOGY

NIHSS

1 – 0-4

2 – 5-15

3 – 16-20

4 – 21-42